EPA Reg. No. 91384-3

PROCESSING REQUEST

Reg # 91384-3 **Decision #** 511951

Description: new product

Electronic Label & Letter (see PPLS):	OR	**Non Electronic Label & Letter** (Scanning required):
☒ Dated: 9/26/16		☐ Dated:

Only one label type should be selected

Other Materials Sent (see jacket):

☒ New CSF(s) Dated: Basic 12/23/15

☐ Other:

File this coversheet and attached materials in the jacket. It must be well organized and clipped together, NOT STAPLED. Then give the jacket with the coversheet and materials to staff in the Information Services Center (ISC) (Room S-4900). If a jacket is full or only available as an image, please file materials in a new jacket and bring it down to the (ISC). For further information please call 703-605-0716.

Reviewer: Elizabeth Fertich

Division: RD/IVB1

Phone: 347-8560 **Date:** 9/27/16

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Registration Division (7505P)
1200 Pennsylvania Ave., N.W
Washington, D.C. 20460

NOTICE OF PESTICIDE:
_X_ Registration
___ Reregistration

(under FIFRA, as amended)

EPA Reg. Number:	Date of Issuance:
91384-3	9/26/16

Term of Issuance:
Conditional, Time-Limited
Expires: 09/26/2018

Name of Pesticide Product:
T2.200 FOR DOGS

Name and Address of Registrant (include ZIP Code):

Richard L. Conn
President, Agent for CAP IM Supply, Inc.
Conn and Smith Inc.
6713 Catskill Road
Lorton, VA 22079-1113

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is conditionally registered in accordance with FIFRA section 3(c)(7)(A). You must comply with the following conditions:

1. Submit and/or cite all data required for registration/reregistration/registration review of your product under FIFRA when the Agency requires all registrants of similar products to submit such data.

Signature of Approving Official:

Laura Bacon, Product Manager 4
Invertebrate and Vertebrate Branch 1,
Registration Division (7505P)

Date: 9/26/16

Office of Pesticide Programs	

EPA Form 8570-6

2. This registration is time-limited and expires 09/26/2018.

3. You must submit quarterly enhanced incident reports and quarterly sales information in doses sold for this product beginning within 3 months of the date the product is first released for shipment, on the first day of the quarter (i.e., January 1, April 1, July 1, or October 1). Please flag any Confidential Business Information as such. Submit enhanced incident reporting and quarterly sales information to the Product Manager's attention. The following is a list of information that must be included in the quarterly reports for each incident:

    - EPA Registration Number
    - Product name (brand name)
    - Lot #
    - Where purchased: internet, store, veterinarian
    - Active Ingredient(s)
    - Weight range for product
    - Date on which incident occurred (mm/dd/yyyy)
    - State in which the incident occurred (standard 2 letter abbreviation)
    - Registrant case #
    - Species: dog, cat, other (specify)
    - Breed: (as reported by pet owner)
    - Age: months or years
    - Sex: M, F, or neutered
    - Weight: pounds
    - Primary Route of Exposure: dermal, oral, other animal, inhalation, other
    - Body System: neurological, dermatological, GI, respiratory, ocular, other
    - Major signs noted with separate column for each sign, using standard terminology
    - Time to Onset: (hours, days)
    - Treated by veterinarian: yes or no
    - First time product used: yes or no
    - Misuse: use on incorrect species, overdose, too frequent dosing, other (describe)
    - Any known precondition
    - EPA Severity Code: death, major, moderate, minor
    - Outcome: died, recovered, still treated, unknown

4. Along with the enhanced incident reporting, you must submit an analysis of the incidents seen, to include the following details:

    - All incidents should be reported including all minor dermal and ocular irritation reports.
    - Summary table for dogs showing number of incidents of each severity code for each route of exposure. Each incident should only be reported once. If one incident has several routes of exposure, the order should be ocular > oral > dermal. In other words, an

incident with both oral and dermal exposure would be reported as oral exposure, and an incident with both ocular and oral exposure would be reported as ocular exposure.

- A similar summary table for cats (misuse or secondary exposure) showing number of incidents of each severity code for each route of exposure.
- Summary table for cats and table for dogs showing number of incidents that are believed due to secondary exposure (e.g., multi-pet households).
- A summary table for dogs showing number of incidents for each severity code for these age ranges: <3 months, 3-6 months, 6-9 months, 9-12 months, 1 yr, 2 yr, 3 yr, 4 yr, 5 yr, 6 yr, 7 yr, 8 yr, 9 yr, 10 yr, 11 yr, 12 yr, 13 yr, 14 yr, 15 yr, >15 yr.
- A summary table showing the number of dog incidents for each severity code for each pet weight range on the product label, as applicable.
- A summary table for dog weight showing number of incidents for each product weight range. This table should show number of incidents in dogs weighing less than that product weight range, number of incidents in dogs in lower half of weight range, number of incidents in dogs in upper half of weight range, and dogs weighing more than the product weight range, as applicable.
- Table showing number of incidents for each dog breed, where provided.
- Table showing number of incidents in dogs for each clinical sign.
- Table showing number of incidents in dogs for each organ system.
- Report aggregate incidents, but do not combine moderate and minor incidents.

If EPA determines that future mitigation measures are necessary for all pet spot-ons, the Agency will inform registrants. If mitigation measures are necessary, EPA may take regulatory action.

5. You are required to comply with the data requirements described in the DCI and EDSP Orders identified below:

   a. Permethrin GDCI-109701-1252
   b. Permethrin GDCI-109701-1281
   c. Permethrin GDCI-109701-1113
   d. Pyriproxyfen GDCI-129032-1299
   e. Imidacloprid GDCI-129099-1516
   f. Imidacloprid GDCI-129099-951
   g. Permethrin EDSP-109701
   h. Pyriproxyfen EDSP-129032
   i. Imidacloprid EDSP-129099

   You must comply with all of the data requirements within the established deadlines. If you have questions about the Generic DCI and EDSP Orders listed above, you may contact the Chemical Review Manager in the Pesticide Reevaluation Division: http://iaspub.epa.gov/apex/pesticides/f?p=chemicalsearch:1

6. Make the following label changes before you release the product for shipment:

- Revise the EPA Registration Number to read, "EPA Reg. No. 91384-3."

7. Submit one copy of the final printed label for the record before you release the product for shipment.

Should you wish to add/retain a reference to the company's website on your label, then please be aware that the website becomes labeling under the Federal Insecticide Fungicide and Rodenticide Act and is subject to review by the Agency. If the website is false or misleading, the product would be misbranded and unlawful to sell or distribute under FIFRA section 12(a)(1)(E). 40 CFR 156.10(a)(5) list examples of statements EPA may consider false or misleading. In addition, regardless of whether a website is referenced on your product's label, claims made on the website may not substantially differ from those claims approved through the registration process. Therefore, should the Agency find or if it is brought to our attention that a website contains false or misleading statements or claims substantially differing from the EPA approved registration, the website will be referred to the EPA's Office of Enforcement and Compliance.

If you fail to satisfy these data requirements, EPA will consider appropriate regulatory action including, among other things, cancellation under FIFRA section 6(e). Your release for shipment of the product constitutes acceptance of these conditions. A stamped copy of the label is enclosed for your records.

Please note that the record for this product currently contains the following CSFs:

- Basic CSF dated 12/23/2015

If you have any questions, you may contact Elizabeth Fertich at 703-347-8560 or via email at fertich.elizabeth@epa.gov.

Sincerely,

Laura N. Bacon, Acting Product Manager 4
Invertebrate & Vertebrate Branch 1 (IVB1)
Registration Division (7505P)
Office of Pesticide Programs

NOTE TO REVIEWER: [(Optional text appears in brackets and parenthesis - the final label may include some or all of the optional text on front, back, side, or inside label panels. Optional marketing claims: see lists at the end of the label)]

Label Directions and Container (Carton, Overwrap of 2 x 3-Count, 2 x 4-Count, 2 x 6-Count, and 3 x 4-Count Cartons), Package Insert, Blister, and Reminder Stickers for

3 x 0.014 FL. OZ. PACKAGE
3 x 0.034 FL. OZ. PACKAGE
3 x 0.084 FL. OZ. PACKAGE
3 x 0.135 FL. OZ. PACKAGE

4 x 0.014 FL. OZ. PACKAGE
4 x 0.034 FL. OZ. PACKAGE
4 x 0.084 FL. OZ. PACKAGE
4 x 0.135 FL. OZ. PACKAGE

6 x 0.014 FL. OZ. PACKAGE
6 x 0.034 FL. OZ. PACKAGE
6 x 0.084 FL. OZ. PACKAGE
6 x 0.135 FL. OZ. PACKAGE

8 x 0.014 FL. OZ. PACKAGE
8 x 0.034 FL. OZ. PACKAGE
8 x 0.084 FL. OZ. PACKAGE
8 x 0.135 FL. OZ. PACKAGE

(FRONT PANEL OF 2 x 3-COUNT, 2 X 4-COUNT, 2 X 6-COUNT, AND 3 X 4-COUNT OVERWRAP)

T2.200 for Dogs

Alternate Brand Names

[ADV Advecta for Dogs]
[ADV Advecta 2 for Dogs]
[ADV Advecta II for Dog
[ADV Advecta 3 for Dogs]
[ADV Advecta III for Dog
[ADV PetAction for Dogs]
[ADV PetAction 2 for Dogs]
[ADV PetAction II for Dogs]
[ADV PetAction 3 for Dogs]
[ADV PetAction III for Dogs]
[ADV PetLock for Dogs]
[ADV PetLock 2 for Dogs]
[ADV PetLock II for Dogs]
[ADV PetLock 3 for Dogs]
[ADV PetLock III for Dogs]
[Advecta 3 for Dogs]
[Advecta K9]
[K9 Advecta (Advanced)]
[Advecta III for Dogs]
[Advecta ADV for Dogs]
[Advecta ADV 2 for Dogs]
[Advecta ADV II for Dogs]
[Advecta ADV 3 for Dogs]
[Advecta ADV III for Dogs]
[Advecta Complete for Dogs]

ACCEPTED
09/26/2016
Under the Federal Insecticide, Fungicide and Rodenticide Act as amended, for the pesticide registered under EPA Reg. No. 91384-3

[Advecta Max for Dogs]
[Advecta Ticks for Dogs]
[Advecta Tix for Dogs]
[K9 Advecta Tix]
[Advecta Tix K9]
[Canine Advecta Tix]
[Advecta Tix Canine]
[Advecta Total for Dogs]
[K9 Advecta Total]
[Canine Advecta Total]
[Advecta Total K9]
[Advecta Total Canine]
[Advectix for Dogs]
[Advectix K9]
[K9 Advectix]
[Advectix Canine]
[Canine Advectix]
[Advectix 2 for Dogs]
[K9 Advectix 2]
[Advectix K9]
[Canine Advectix 2]
[Advectix Canine 2]
[Advectix II for Dogs]
[K9 Advectix II]
[Advectix II K9]
[Canine Advectix II]
[Advectix II Canine]
[Advectix 3 for Dogs]
[K9 Advectix 3]
[Advectix 3 K9]
[Canine Advectix 3]
[Advectix 3 Canine]
[Advectix III for Dogs]
[K9 Advectix III]
[Advectix III K9]
[Canine Advectix III]
[Advectix III Canine]
[Para|Defense 3 for Dogs]
[K9 Para|Defense 3]
[Canine Para|Defense 3]
[Para|Defense K9 3]
[Para|Defense Canine 3]
[Para|Defense Advanced for Dogs]
[K9 Para|Defense Advanced]
[Canine Para|Defense Advanced]
[Para|Defense K9 Advanced]
[Para|Defense Canine Advanced]
[Para|Defense Complete for Dogs]
[K9 Para|Defense Complete]
[Canine Para|Defense Complete]
[Para|Defense K9 Complete]
[Para|Defense Canine Complete]
[Para|Defense Extra for Dogs]
[K9 Para|Defense Extra]
[Canine Para|Defense Extra]
[Para|Defense Extra K9]
[Para|Defense Extra Canine]

[Para|Defense Flea & Tick for Dogs]
[K9 Para|Defense Flea & Tick]
[Canine Para|Defense Flea & Tick]
[Para|Defense Flea & Tick K9]
[Para|Defense Flea & Tick Canine]
[Para|Defense III for Dogs]
[K9 Para|Defense III]
[Canine Para|Defense III]
[Para|Defense III K9]
[Para|Defense Canine III]
[Para|Defense Max for Dogs]
[K9 Para|Defense Max]
[Canine Para|Defense Max]
[Para|Defense Max K9]
[Para|Defense Canine Max]
[Para|Defense Plus Tick Control for Dogs]
[K9 Para|Defense Plus Tick Control]
[Para|Defense Pro for Dogs]
[K9 Para|Defense Pro]
[Canine Para|Defense Pro]
[Para|Defense Pro K9]
[Para|Defense Canine Pro]
[Para|Defense Multi-Vector]
[K9 Para|Defense Multi-Vector]
[Canine Para|Defense Multi-Vector]
[Para|Defense Multi-Vector K9]
[Para|Defense Canine Multi-Vector]
[Para|Defense Plus Ticks for Dogs]
[K9 Para|Defense Plus]
[Canine Para|Defense Plus]
[Para|Defense Plus K9]
[Para|Defense Plus Canine]
[Para|Defense Tix for Dogs]
[K9 Para|Defense Tix]
[Canine Para|Defense Tix]
[Para|Defense Tix K9]
[Para|Defense Canine Tix]
[PetAction 3 for Dogs]
[PetAction 3 K9]
[PetAction 3 Canine]
[K9 PetAction 3]
[Canine PetAction 3]
[PetAction III for Dogs]
[PetAction III K9]
[PetAction III Canine]
[K9 PetAction III]
[Canine PetAction III]
[PetAction K9 (Advanced)]
[K9 PetAction (Advanced)]
[PetAction ADV for Dogs]
[PetAction ADV K9]
[PetAction ADV Canine]
[K9 PetAction ADV]
[Canine PetAction ADV]
[PetAction ADV 2 for Dogs]
[K9 PetAction ADV]
[Canine PetAction ADV]

[PetAction ADV II for Dogs]
[K9 PetAction ADV II]
[Canine PetAction ADV II]
[PetAction ADV 3 for Dogs]
[K9 PetAction ADV 3]
[Canine PetAction ADV 3]
[PetAction ADV III for Dogs]
[K9 PetAction ADV III]
[Canine PetAction ADV III]
[PetAction Complete for Dogs]
[K9 PetAction Complete]
[Canine PetAction Complete]
[PetAction Max for Dogs]
[K9 PetAction Max]
[Canine PetAction Max]
[PetAction Ticks for Dogs]
[K9 PetAction Ticks]
[Canine PetAction Ticks]
[PetAction Tix for Dogs]
[K9 PetAction Tix]
[Canine PetAction Tix]
[PetAction Total for Dogs]
[K9 PetAction Total]
[Canine PetAction Total]
[PetLock 3 for Dogs]
[K9 PetLock 3]
[Canine PetLock 3]
[PetLock 3 K9]
[PetLock 3 Canine]
[PetLock K9]
[K9 PetLock]
[PetLock III for Dogs]
[K9 PetLock III]
[Canine PetLock III]
[PetLock III K9]
[PetLock III Canine]
[PetLock ADV for Dogs]
[K9 PetLock DV]
[Canine PetLock ADV]
[PetLock ADV K9]
[PetLock ADV Canine]
[PetLock ADV 2 for Dogs]
[K9 PetLock ADV 2]
[PetLock ADV 2 Canine]
[PetLock ADV II for Dogs]
[K9 PetLock ADV II]
[PetLock ADV II Canine]
[PetLock ADV 3 for Dogs]
[K9 PetLock ADV 3]
[PetLock ADV III for Dogs]
[K9 PetLock ADV III]
[PetLock ADV III Canine]
[PetLock Complete for Dogs]
[PetLock Max for Dogs]
[PetLock Ticks for Dogs]
[K9 PetLock Ticks]
[Canine PetLock Ticks]

[PetLock Tix for Dogs]
[PetLock tix K9]
[PetLock Tix Canine]
[PetLock Total for Dogs]
[K9 PetLock Total]
[Canine PetLock Total]
[PetLock Total K9]
[PetLock Total Canine]
[K9 Lock II]

Monthly topical treatment and prevention of ticks, fleas, mosquitos, biting flies, and lice.
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 5-10 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 11-20 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 21-55 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing over 55 lbs.]

KEEP OUT OF REACH OF CHILDREN
WARNING

Active Ingredients	% By Weight
Imidacloprid	8.80%
Permethrin*	44.00%
Pyriproxyfen	0.44%
Other Ingredients	46.76%
Total	100.00%

*cis/trans ratio: Max 55(±) cis and min 45%(±) trans

See back panel for Precautionary Statements
See package insert for Directions for Use, Storage and Disposal, and First Aid information.

DO NOT USE ON CATS

(THE CATS ICON WILL BE YELLOW OR CONTRASTING COLOR TO PACKAGING)

Net Contents:
[2 cartons of [0.042 fl. oz.][0.056 fl. oz.][0.084 fl. oz.] ([3,4,6] applicators each containing 0.014 fl. oz (0.4 mL), [3,4,6] doses per carton, [6,8,12] doses total)]
[2 cartons of [0.102 fl. oz.][0.136 fl. oz.][0.204 fl. oz.] ([3,4,6] applicators each containing 0.034 fl. oz (1.0 mL), [3,4,6] doses per carton, [6,8,12] doses total)]
[2 cartons of [0.255 fl. oz.][0.34 fl. oz.][0.51 fl. oz.] ([3,4,6] applicators each containing 0.084 fl. oz (2.5 mL), [3,4,6] doses per carton, [6,8,12] doses total)]
[2 cartons of [0.405 fl. oz.][0.54 fl. oz.][0.81 fl. oz.] ([3,4,6] applicators each containing 0.135 fl. oz (4.0 mL), [3,4,6] doses per carton, [6,8,12] doses total)]
[3 cartons of [0.056 fl. oz.] (4 applicators each containing 0.014 fl. oz (0.4 mL), 4 doses per carton, 12 doses total)]
[3 cartons of [0.136 fl. oz.] (4 applicators each containing 0.034 fl. oz (1.0 mL)], 4 doses per carton, 12 doses total)]
[3 cartons of [0.34 fl. oz.] (4 applicators each containing 0.084 fl. oz (2.5 mL)], 4 doses per carton, 12 doses total)]
[3 cartons of [0.54 fl. oz.] (4 applicators each containing 0.135 fl. oz (4.0 mL)], 4 doses per carton, 12 doses total)]

(FRONT PANEL OF CARTON)

T2.200 for Dogs

Alternate Brand Names

[ADV Advecta for Dogs]
[ADV Advecta 2 for Dogs]
[ADV Advecta II for Dog
[ADV Advecta 3 for Dogs]
[ADV Advecta III for Dog
[ADV PetAction for Dogs]
[ADV PetAction 2 for Dogs]
[ADV PetAction II for Dogs]
[ADV PetAction 3 for Dogs]
[ADV PetAction III for Dogs]
[ADV PetLock for Dogs]
[ADV PetLock 2 for Dogs]
[ADV PetLock II for Dogs]
[ADV PetLock 3 for Dogs]
[ADV PetLock III for Dogs]
[Advecta 3 for Dogs]
[Advecta K9]
[K9 Advecta (Advanced)]
[Advecta III for Dogs]
[Advecta ADV for Dogs]
[Advecta ADV 2 for Dogs]
[Advecta ADV II for Dogs]
[Advecta ADV 3 for Dogs]
[Advecta ADV III for Dogs]
[Advecta Complete for Dogs]
[Advecta Max for Dogs]
[Advecta Ticks for Dogs]
[Advecta Tix for Dogs]
[K9 Advecta Tix]
[Advecta Tix K9]
[Canine Advecta Tix]
[Advecta Tix Canine]
[Advecta Total for Dogs]
[K9 Advecta Total]
[Canine Advecta Total]
[Advecta Total K9]
[Advecta Total Canine]
[Advectix for Dogs]
[Advectix K9]
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[Advectix Canine]
[Canine Advectix]
[Advectix 2 for Dogs]
[K9 Advectix 2]
[Advectix K9]
[Canine Advectix 2]
[Advectix Canine 2]
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[K9 Advectix II]
[Advectix II K9]
[Canine Advectix II]

[Advectix II Canine]
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[K9 Advectix 3]
[Advectix 3 K9]
[Canine Advectix 3]
[Advectix 3 Canine]
[Advectix III for Dogs]
[K9 Advectix III]
[Advectix III K9]
[Canine Advectix III]
[Advectix III Canine]
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[K9 Para|Defense 3]
[Canine Para|Defense 3]
[Para|Defense K9 3]
[Para|Defense Canine 3]
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[Canine Para|Defense Advanced]
[Para|Defense K9 Advanced]
[Para|Defense Canine Advanced]
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[Canine Para|Defense Complete]
[Para|Defense K9 Complete]
[Para|Defense Canine Complete]
[Para|Defense Extra for Dogs]
[K9 Para|Defense Extra]
[Canine Para|Defense Extra]
[Para|Defense Extra K9]
[Para|Defense Extra Canine]
[Para|Defense Flea & Tick for Dogs]
[K9 Para|Defense Flea & Tick]
[Canine Para|Defense Flea & Tick]
[Para|Defense Flea & Tick K9]
[Para|Defense Flea & Tick Canine]
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[K9 Para|Defense III]
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[Canine Para|Defense Max]
[Para|Defense Max K9]
[Para|Defense Canine Max]
[Para|Defense Plus Tick Control for Dogs]
[Para|Defense Pro for Dogs]
[K9 Para|Defense Pro]
[Canine Para|Defense Pro]
[Para|Defense Pro K9]
[Para|Defense Canine Pro]
[Para|Defense Multi-Vector]
[K9 Para|Defense Multi-Vector]
[Canine Para|Defense Multi-Vector]
[Para|Defense Multi-Vector K9]
[Para|Defense Canine Multi-Vector]

[Para|Defense Plus Ticks for Dogs]
[K9 Para|Defense Plus]
[Canine Para|Defense Plus]
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[Canine Para|Defense Tix]
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[PetAction 3 Canine]
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[Canine PetAction 3]
[PetAction III for Dogs]
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[PetAction III Canine]
[K9 PetAction III]
[Canine PetAction III]
[PetAction K9 (Advanced)]
[K9 PetAction (Advanced)]
[PetAction ADV for Dogs]
[PetAction ADV K9]
[PetAction ADV Canine]
[K9 PetAction ADV]
[Canine PetAction ADV]
[PetAction ADV 2 for Dogs]
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[Canine PetAction ADV]
[PetAction ADV II for Dogs]
[K9 PetAction ADV II]
[Canine PetAction ADV II]
[PetAction ADV 3 for Dogs]
[K9 PetAction ADV 3]
[Canine PetAction ADV 3]
[PetAction ADV III for Dogs]
[K9 PetAction ADV III]
[Canine PetAction ADV III]
[PetAction Complete for Dogs]
[K9 PetAction Complete]
[Canine PetAction Complete]
[PetAction Max for Dogs]
[K9 PetAction Max]
[Canine PetAction Max]
[PetAction Ticks for Dogs]
[K9 PetAction Ticks]
[Canine PetAction Ticks]
[PetAction Tix for Dogs]
[K9 PetAction Tix]
[Canine PetAction Tix]
[PetAction Total for Dogs]
[K9 PetAction Total]
[Canine PetAction Total]
[PetLock 3 for Dogs]
[K9 PetLock 3]
[Canine PetLock 3]

[PetLock 3 K9]
[PetLock 3 Canine]
[PetLock K9]
[K9 PetLock]
[PetLock III for Dogs]
[K9 PetLock III]
[Canine PetLock III]
[PetLock III K9]
[PetLock III Canine]
[PetLock ADV for Dogs]
[K9 PetLock DV]
[Canine PetLock ADV]
[PetLock ADV K9]
[PetLock ADV Canine]
[PetLock ADV 2 for Dogs]
[K9 PetLock ADV 2]
[PetLock ADV 2 Canine]
[PetLock ADV II for Dogs]
[K9 PetLock ADV II]
[PetLock ADV II Canine]
[PetLock ADV 3 for Dogs]
[K9 PetLock ADV 3]
[PetLock ADV III for Dogs]
[K9 PetLock ADV III]
[PetLock ADV III Canine]
[PetLock Complete for Dogs]
[PetLock Max for Dogs]
[PetLock Ticks for Dogs]
[K9 PetLock Ticks]
[Canine PetLock Ticks]
[PetLock Tix for Dogs]
[PetLock tix K9]
[PetLock Tix Canine]
[PetLock Total for Dogs]
[K9 PetLock Total]
[Canine PetLock Total]
[PetLock Total K9]
[PetLock Total Canine]
[K9 Lock II]

Monthly topical treatment and prevention of ticks, fleas, mosquitos, biting flies, and lice.

[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 5-10 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 11-20 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 21-55 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing over 55 lbs.]

KEEP OUT OF REACH OF CHILDREN
WARNING

Active Ingredients	% By Weight
Imidacloprid	8.80%
Permethrin*	44.00%
Pyriproxyfen	0.44%
Other Ingredients	46.76%
Total	100.00%

*cis/trans ratio: Max 55(±) cis and min 45%(±) trans

See back panel for Precautionary Statements
See package insert for Directions for Use, Storage and Disposal, and First Aid information.

DO NOT USE ON CATS

(THE CATS ICON WILL BE YELLOW OR CONTRASTING COLOR TO PACKAGING)

Net Contents:
[0.042 fl. oz.][0.056 fl. oz.][0.084 fl. oz.][0.112 fl. oz.] [3,4,6,8] applicators each containing 0.014 fl. oz (0.4 mL)]
[0.102 fl. oz.][0.136 fl. oz.][0.204 fl. oz.][0.272 fl. oz.] [3,4,6,8] applicators each containing 0.034 fl. oz (1.0 mL)]
[0.255 fl. oz.][0.34 fl. oz.][0.51 fl. oz.][0.68 fl. oz.] [3,4,6,8] applicators each containing 0.084 fl. oz (2.5 mL)]
[0.405 fl. oz.][0.54 fl. oz.][0.81 fl. oz.][1.08 fl. oz.] [3,4,6,8] applicators each containing 0.135 fl. oz (4.0 mL)]

(BACK PANEL OF CARTON AND OF OVERWRAP OF 2 X 3-COUNT, 2 X 4-COUNT, 2 X 6-COUNT, AND 3 X 4-COUNT CARTONS)

T2.200 for Dogs

Monthly topical treatment and prevention of ticks, fleas, mosquitos, biting flies, and lice.
[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing 5-10 lbs.]
[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing 11-20 lbs.]
[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing 21-55 lbs.]
[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing over 55 lbs.]
READ THE ENTIRE LABEL BEFORE EACH USE

Monthly topical treatment and prevention of ticks, fleas, mosquitos, biting flies, and lice on Dogs

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS
WARNING. Causes substantial but temporary eye injury. Do not get in eyes or on clothing. Harmful if swallowed. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Remove and wash contaminated clothing before reuse.

HAZARDS TO DOMESTIC ANIMALS
For external use on dogs only. Do not use on animals other than dogs. Do not use on puppies under seven (7) weeks of age [or weighing less than 5 pounds]. Do not get this product in dog's eyes or mouth. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing animals. Individual sensitivities may occur after using ANY pesticide product for dogs. If signs persist, or become more severe, consult a veterinarian immediately. If your animal is on medication, consult your veterinarian before using this or any other product.

ENVIRONMENTAL HAZARDS
This pesticide is extremely toxic to aquatic organisms, including fish and invertebrates. Do not add directly to water. Do not contaminate water when disposing of product or packaging.

Side Effects:
Monitor your dog after application. Side effects may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as vomiting or diarrhea have also been reported. If these or other side effects (such as lethargy or agitation) occur, consult your veterinarian or call 1-xxx-xxx-xxxx.

DO NOT USE ON CATS – MAY BE FATAL. Keep cats away from treated dogs for 24 hours. If applied to a cat or ingested by a cat, contact your veterinarian immediately.

For consumer questions call 1-8XX-XXX-XXXX
For medical emergencies call 1-xxx-xxx-xxxx

CAP IM Supply, Inc.
303 Perimeter Center North, Suite 300
Atlanta, GA 30346

EPA Est. No. XXXXX-XX-X

EPA Reg No. 91384-XXX

[Sample – Not for (Re)Sale]

[Store Use Only]

(SIDE PANELS OF CARTON AND OF OVERWRAP OF 2 X 3-COUNT, 2 X 4-COUNT, 2 X 6-COUNT, AND 3 X 4-COUNT CARTONS)

[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing 5-10 lbs.]
[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing 11-20 lbs.]
[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing 21-55 lbs.]
[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing over 55 lbs.]

[T2.200 for Dogs]

[EPA Reg. No. 91384-xxx]
Lot/Batch Number

(PACKAGE INSERT LABELING)

T2.200 for Dogs

Alternate Brand Names

[ADV Advecta for Dogs]
[ADV Advecta 2 for Dogs]
[ADV Advecta II for Dog
[ADV Advecta 3 for Dogs]
[ADV Advecta III for Dog
[ADV PetAction for Dogs]
[ADV PetAction 2 for Dogs]
[ADV PetAction II for Dogs]
[ADV PetAction 3 for Dogs]
[ADV PetAction III for Dogs]
[ADV PetLock for Dogs]
[ADV PetLock 2 for Dogs]
[ADV PetLock II for Dogs]
[ADV PetLock 3 for Dogs]
[ADV PetLock III for Dogs]
[Advecta 3 for Dogs]
[Advecta K9]
[K9 Advecta (Advanced)]
[Advecta III for Dogs]
[Advecta ADV for Dogs]
[Advecta ADV 2 for Dogs]
[Advecta ADV II for Dogs]
[Advecta ADV 3 for Dogs]
[Advecta ADV III for Dogs]
[Advecta Complete for Dogs]
[Advecta Max for Dogs]
[Advecta Ticks for Dogs]
[Advecta Tix for Dogs]
[K9 Advecta Tix]
[Advecta Tix K9]
[Canine Advecta Tix]
[Advecta Tix Canine]
[Advecta Total for Dogs]
[K9 Advecta Total]
[Canine Advecta Total]
[Advecta Total K9]
[Advecta Total Canine]
[Advectix for Dogs]
[Advectix K9]
[K9 Advectix]
[Advectix Canine]
[Canine Advectix]
[Advectix 2 for Dogs]
[K9 Advectix 2]
[Advectix K9]
[Canine Advectix 2]
[Advectix Canine 2]
[Advectix II for Dogs]
[K9 Advectix II]
[Advectix II K9]
[Canine Advectix II]

[Advectix II Canine]
[Advectix 3 for Dogs]
[K9 Advectix 3]
[Advectix 3 K9]
[Canine Advectix 3]
[Advectix 3 Canine]
[Advectix III for Dogs]
[K9 Advectix III]
[Advectix III K9]
[Canine Advectix III]
[Advectix III Canine]
[Para|Defense 3 for Dogs]
[K9 Para|Defense 3]
[Canine Para|Defense 3]
[Para|Defense K9 3]
[Para|Defense Canine 3]
[Para|Defense Advanced for Dogs]
[K9 Para|Defense Advanced]
[Canine Para|Defense Advanced]
[Para|Defense K9 Advanced]
[Para|Defense Canine Advanced]
[Para|Defense Complete for Dogs]
[K9 Para|Defense Complete]
[Canine Para|Defense Complete]
[Para|Defense K9 Complete]
[Para|Defense Canine Complete]
[Para|Defense Extra for Dogs]
[K9 Para|Defense Extra]
[Canine Para|Defense Extra]
[Para|Defense Extra K9]
[Para|Defense Extra Canine]
[Para|Defense Flea & Tick for Dogs]
[K9 Para|Defense Flea & Tick]
[Canine Para|Defense Flea & Tick]
[Para|Defense Flea & Tick K9]
[Para|Defense Flea & Tick Canine]
[Para|Defense III for Dogs]
[K9 Para|Defense III]
[Canine Para|Defense III]
[Para|Defense III K9]
[Para|Defense Canine III]
[Para|Defense Max for Dogs]
[K9 Para|Defense Max]
[Canine Para|Defense Max]
[Para|Defense Max K9]
[Para|Defense Canine Max]
[Para|Defense Plus Tick Control for Dogs]
[Para|Defense Pro for Dogs]
[K9 Para|Defense Pro]
[Canine Para|Defense Pro]
[Para|Defense Pro K9]
[Para|Defense Canine Pro]
[Para|Defense Multi-Vector]
[K9 Para|Defense Multi-Vector]
[Canine Para|Defense Multi-Vector]
[Para|Defense Multi-Vector K9]
[Para|Defense Canine Multi-Vector]

[Para|Defense Plus Ticks for Dogs]
[K9 Para|Defense Plus]
[Canine Para|Defense Plus]
[Para|Defense Plus K9]
[Para|Defense Plus Canine]
[Para|Defense Tix for Dogs]
[K9 Para|Defense Tix]
[Canine Para|Defense Tix]
[Para|Defense Tix K9]
[Para|Defense Canine Tix]
[PetAction 3 for Dogs]
[PetAction 3 K9]
[PetAction 3 Canine]
[K9 PetAction 3]
[Canine PetAction 3]
[PetAction III for Dogs]
[PetAction III K9]
[PetAction III Canine]
[K9 PetAction III]
[Canine PetAction III]
[PetAction K9 (Advanced)]
[K9 PetAction (Advanced)]
[PetAction ADV for Dogs]
[PetAction ADV K9]
[PetAction ADV Canine]
[K9 PetAction ADV]
[Canine PetAction ADV]
[PetAction ADV 2 for Dogs]
[K9 PetAction ADV]
[Canine PetAction ADV]
[PetAction ADV II for Dogs]
[K9 PetAction ADV II]
[Canine PetAction ADV II]
[PetAction ADV 3 for Dogs]
[K9 PetAction ADV 3]
[Canine PetAction ADV 3]
[PetAction ADV III for Dogs]
[K9 PetAction ADV III]
[Canine PetAction ADV III]
[PetAction Complete for Dogs]
[K9 PetAction Complete]
[Canine PetAction Complete]
[PetAction Max for Dogs]
[K9 PetAction Max]
[Canine PetAction Max]
[PetAction Ticks for Dogs]
[K9 PetAction Ticks]
[Canine PetAction Ticks]
[PetAction Tix for Dogs]
[K9 PetAction Tix]
[Canine PetAction Tix]
[PetAction Total for Dogs]
[K9 PetAction Total]
[Canine PetAction Total]
[PetLock 3 for Dogs]
[K9 PetLock 3]
[Canine PetLock 3]

[PetLock 3 K9]
[PetLock 3 Canine]
[PetLock K9]
[K9 PetLock]
[PetLock III for Dogs]
[K9 PetLock III]
[Canine PetLock III]
[PetLock III K9]
[PetLock III Canine]
[PetLock ADV for Dogs]
[K9 PetLock DV]
[Canine PetLock ADV]
[PetLock ADV K9]
[PetLock ADV Canine]
[PetLock ADV 2 for Dogs]
[K9 PetLock ADV 2]
[PetLock ADV 2 Canine]
[PetLock ADV II for Dogs]
[K9 PetLock ADV II]
[PetLock ADV II Canine]
[PetLock ADV 3 for Dogs]
[K9 PetLock ADV 3]
[PetLock ADV III for Dogs]
[K9 PetLock ADV III]
[PetLock ADV III Canine]
[PetLock Complete for Dogs]
[PetLock Max for Dogs]
[PetLock Ticks for Dogs]
[K9 PetLock Ticks]
[Canine PetLock Ticks]
[PetLock Tix for Dogs]
[PetLock tix K9]
[PetLock Tix Canine]
[PetLock Total for Dogs]
[K9 PetLock Total]
[Canine PetLock Total]
[PetLock Total K9]
[PetLock Total Canine]
[K9 Lock II]

Monthly topical treatment and prevention of ticks, fleas, mosquitos, biting flies, and lice.

[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 5-10 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 11-20 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 21-55 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing over 55 lbs.]

Active Ingredients	% By Weight
Imidacloprid	8.80%
Permethrin*	44.00%
Pyriproxyfen	0.44%
Other Ingredients	46.76%
Total	100.00%

*cis/trans ratio: Max 55(±) cis and min 45%(±) trans

KEEP OUT OF REACH OF CHILDREN
WARNING

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS

WARNING. Causes substantial but temporary eye injury. Do not get in eyes or on clothing. Harmful if swallowed. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Remove and wash contaminated clothing before reuse.

HAZARDS TO DOMESTIC ANIMALS

For external use on dogs only. Do not use on animals other than dogs. Do not use on puppies under seven (7) weeks of age [or weighing less than 5 pounds]. Do not get this product in dog's eyes or mouth. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing animals. Individual sensitivities may occur after using ANY pesticide product for dogs. If signs persist, or become more severe, consult a veterinarian immediately. If your animal is on medication, consult your veterinarian before using this or any other product.

ENVIRONMENTAL HAZARDS

This pesticide is extremely toxic to aquatic organisms, including fish and invertebrates. Do not add directly to water. Do not contaminate water when disposing of product or packaging.

Side Effects:

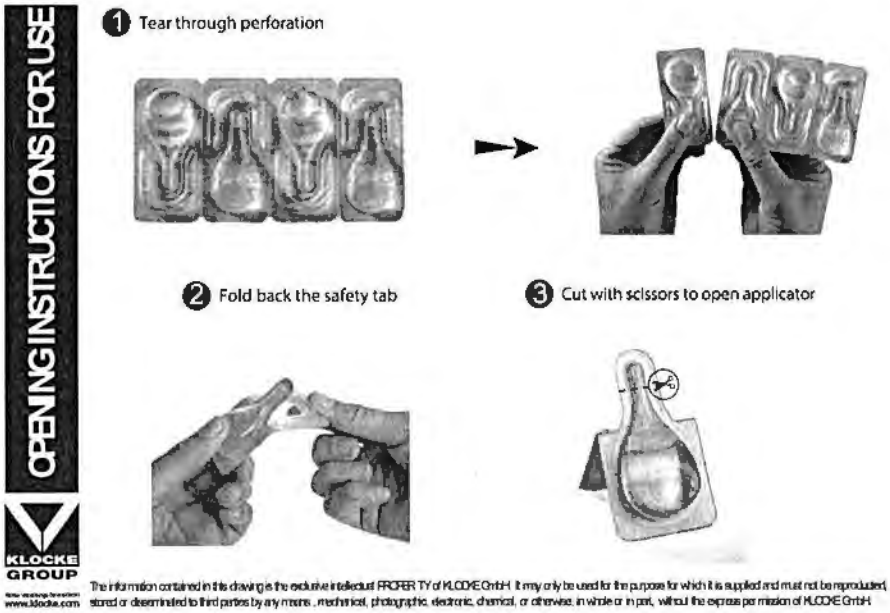
Monitor your dog after application. Side effects may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as vomiting or diarrhea have also been reported. If these or other side effects (such as lethargy or agitation) occur, consult your veterinarian or call 1-xxx-xxx-xxxx.

FIRST AID	
If In Eyes:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If Swallowed:	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything by mouth to an unconscious person.
HOT LINE NUMBER	
Have the product container or label with you when calling a poison control center or doctor, or going for treatment. For medical emergencies call 1-xxx-xxx-xxxx. For consumer questions, call 1-xxx-xxx-xxxx	
NOTE TO PHYSICIAN	
Treat the patient symptomatically.	

DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling. Do not contaminate feed or food.

HOW TO OPEN

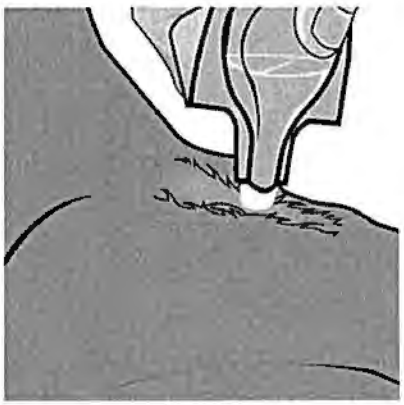


NOTE TO REVIEWER: When this product is packaged as the 3-count or 6-count version, the above image will show a 3-count applicator strip instead of the 4-count as shown above.

Repeat steps 1 to 3 for each applicator.

HOW TO APPLY

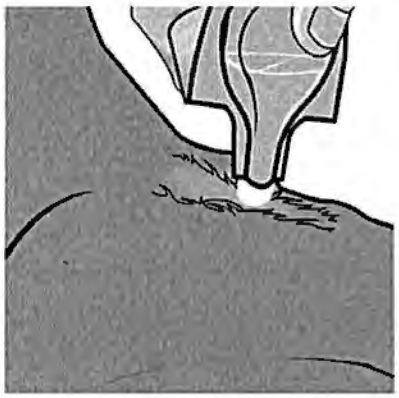
1. Prepare applicator as shown in "How to Open".
2. 5 – 10 lbs and 11-20 lbs. [Apply the entire contents of the applicator to one spot [as shown]:
   NOTE TO REVIEWER: The following visual is optional.

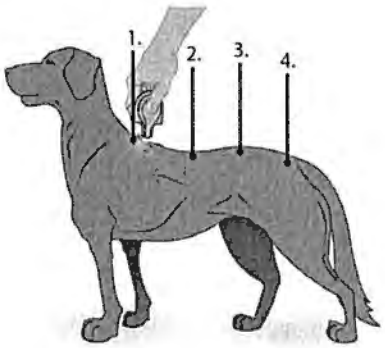


Part the hair on the dog back between the shoulder blades until the skin is visible. Place the tip of the applicator on the skin and gently squeeze to apply all the contents to the skin.] [Part the dog's hair and

place the tip of the applicator [tube][pipette] behind the neck and between the shoulders. Squeeze the applicator [tube][pipette] thoroughly so that the entire contents are applied to one spot.] Carefully avoid allowing the product to run off the side of the dog. Keep solution out of your dog's eyes and do not allow your dog to ingest this product.]21 – 55 lbs. and Over 55 lbs. Apply the entire contents of the applicator evenly to three or four spots on the top of the back of the dog from the shoulder to the base of the tail [as shown]:

NOTE TO REVIEWER: The following visual is optional.





At each application site part the hair of the dog until the skin is visible. Place the tip of the applicator on the skin and gently squeeze to apply the solution on the skin. Do not apply an amount of solution at any one spot that could cause some of the solution to run off the side of the dog. Keep solution out of your dog's eyes and do not allow your dog to ingest this product..

3. Discard empty applicator and packaging as described in the Storage and Disposal section.

4. Under normal conditions the product remains effective for a month. In cases of severe flea infestation, retreatment may be necessary earlier than one month. Do not reapply T2.200 more often than once every seven (7) days. Once flea control is attained, return to a monthly application [dose] schedule.

PRODUCT INFORMATION

The successive feeding activity of fleas on dogs may elicit a hypersensitivity skin disorder known as flea allergy dermatitis (FAD). Treatment of dogs with T2.200 rapidly kills fleas and may reduce the incidence of this condition.

T2.200 kills existing fleas on dogs within 12 hours. Reinfesting fleas are killed within 2 hours with protection against further flea infestation lasting at least four (4) weeks. Pre-existing pupae in the environment may continue to emerge for six (6) weeks or longer depending upon the climatic conditions.

T2.200 is waterproof and remains effective following a shampoo [treatment], swimming or after exposure to rain or sunlight.

Monthly treatments are required for optimal control and prevention of fleas and ticks.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Pesticide Storage: Store in a cool, dry place. Protect from freezing. **Pesticide Disposal and Container Handling:** Non refillable container. **If empty:** Do not reuse this container. Place in trash or offer for recycling if available. **If partly filled:** Call your local solid waste agency for disposal instructions. Never place unused product down any indoor or outdoor drain.

NOTE TO REVIEWER: A warranty statement of any kind is optional, but if a warranty statement is used, the following two alternative options are proposed:

[LIMITED WARRANTY AND LIMITATION OF DAMAGES

IMPORTANT: READ BEFORE USE. Read the entire Directions for Use, Conditions of Warranties and Limitations of Liability before using this product. If these terms and conditions are not acceptable, return the unopened product container at once. By using this product, user or buyer accepts the following Disclaimer of Warranties and Limitations of Liability.

CONDITIONS: The directions for use of this product are believed to be adequate and must be followed carefully. However, it is impossible to eliminate all risks associated with the use of this product. Ineffectiveness, injury, and other unintended consequences may result because of such factors as manner of use or application (including misuse), the presence of other materials, weather conditions, and other unknown factors, all of which are beyond the control of CAP IM Supply, Inc.. All such risks shall be assumed by the user or buyer.

DISCLAIMER OF WARRANTIES: To the extent consistent with applicable law, CAP IM Supply, Inc. makes no other warranties, express or implied, of merchantability or of fitness for a particular purpose or otherwise, that extend beyond statements on this label.

LIMITATIONS OF LIABILITY: To the extent consistent with applicable law, neither CAP IM Supply, Inc., the manufacturer, nor the Seller shall be liable for any indirect, special, incidental or consequential damages resulting from the use, handling, application, storage, or disposal of this product. To the extent consistent with applicable law, the exclusive remedy of the user or buyer for any and all losses, injuries or damages resulting from the use, handling, application, or storage of this product, whether in contract, warranty, tort, negligence, strict liability or otherwise, shall not exceed the purchase price paid.]

[WARRANTY

To the extent consistent with applicable law, CAP IM Supply, Inc. and/or seller makes no warranty, expressed or implied, concerning the use of this product other than indicated on the label. Buyer assumes all risk of use resulting from the handling of this product. Seller shall return the purchase price or at the election of the seller replace the product.]

NOTE TO REVIEWER: The following optional websites, currently under construction, will go live prior to use on any packaging being released for shipment:
[For more information visit [www.Advecta3.com] [www.PetLockMax.com]]

DO NOT USE ON CATS – MAY BE FATAL. Keep cats away from treated dogs for 24 hours. If applied to a cat or ingested by a cat, contact your veterinarian immediately.

For consumer questions call 1-8XX-XXX-XXXX
For medical emergencies call 1-XXX-XXX-XXXX

EPA Reg No. 91384-XXX

CAP IM Supply, Inc.
303 Perimeter Center North, Suite 300
Atlanta, GA 30346

(LABEL TEXT FOR INDIVIDUAL APPLICATOR)

T2.200 for Dogs

[For external use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 5-10 lbs.]
[For external use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 11-20 lbs.]
[For external use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 21-55 lbs.]
[For external use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing over 55 lbs.]

8.80% imidacloprid
44.00% permethrin
0.44% pyriproxyfen

EPA Reg. No. 91384-XXX

KEEP OUT OF REACH OF CHILDREN

WARNING

DO NOT USE ON CATS

Read the Entire Label Before Use

CAP IM Supply, Inc

[0.014 fl oz (0.4 mL)]
[0.034 fl oz (1.0 mL)]
[0.084 fl oz (2.5 mL)]
[0.135 fl oz (4.0 mL)]

Lot No. 0000000

NOTE TO REVIEWER: [(Brackets and parentheses indicate alternate language)]

OPTIONAL MARKETING CLAIMS

- [For use only on dogs and puppies 7 weeks of age and older and greater than 5 lbs.]
- [T2.200 contains [imidacloprid], [permethrin] and [an/the] [insect growth regulator] [IGR] [pyriproxyfen]]
- [A single topical application [dose] remains effective for [a month][[four](4) weeks]]
- [Convenient, easy to apply [monthly] topical solution]
- [Once a month topical flea treatment for only dogs 7 weeks of age or older and greater than 5 lbs.] [T2.200 is indicated for the prevention and treatment of fleas, ticks, biting flies, mosquitoes [that can transmit disease], and lice only on dogs [7 weeks of age and older and greater than 5 lbs.]]
- [Repels and kills ticks, fleas, and mosquitoes]
- [For the treatment and prevention of flea infestations]
- [One treatment prevents further flea infestations for [a month][[four](4) weeks]]
- [Kills fleas on dogs within 12 hours
- [Continues to prevent infestations for [a month][four](4) weeks]
- [Kills fleas within 12 hours of application]
- [Controls existing flea infestations by rapidly killing adult fleas]
- [Prevents reinfestations by killing adult fleas before they lay eggs]
- [Effectively breaks the flea life cycle]
- [Flea adulticide, larvicide and ovicide]
- [Effectively targets all [life] stages of [fleas] and [ticks]]
- [3-way flea protection] [kills] [controls] [adults], [larvae][, and] [eggs]]
- [Prevents development of fleas, [flea eggs], [pupae] and [larvae] for [a month][[four](4) weeks]]
- [Prevents development of all flea [life] stages [for] [a month][[four](4) weeks]]
- [Repels and kills [all] [life] [stages of fleas]]
- [Prevents flea eggs [and flea larvae] from developing into [biting] [adult] fleas]
- [Treatment with T2.200 rapidly kills fleas and may reduce the incidence of Flea Allergic Dermatitis (FAD)]
- [Repels and kills ticks [including Deer ticks (vector of Lyme disease)], [American dog ticks (vector of Rocky Mountain spotted fever)], [Brown dog ticks (vector of Ehrlichiosis)], and [Lone Star ticks (vector of Ehrlichiosis)] for up to four weeks]
- [Repels and kills mosquitoes [for up to four weeks]]
- [Repels and kills mosquitoes often before they have a chance to take a blood meal]
- [[Prevents blood-feeding by] [Kills and repels][killing and repelling] mosquitoes]
- [Repels and inhibits blood-feeding by biting flies]
- [Repels and prevents blood-feeding by biting flies]
- [Repels [annoying][bothersome][nuisance] biting flies]
- [Inhibits [annoying][bothersome][nuisance] biting flies]
- [[Prevents][inhibits] blood-feeding by biting flies]
- [Remains effective after bathing [and/or swimming]]
- [Remains effective following swimming [and/or shampooing]]
- [Kills [biting][chewing] lice]
- [For treatment and prevention of [biting][chewing] lice [infestations]]
- [Controls existing [biting][chewing] lice infestations]
- [5-way protection against fleas, ticks, biting flies, mosquitoes, and lice]
- [Treats, prevents and controls [biting][chewing] lice [infestations]]
- [Provides effective control of [biting][chewing] lice [infestations]]
- [Kills [biting][chewing] lice and prevents further infestations]
- [For treatment and prevention of infestations with [biting][chewing] lice]
- [Waterproof]
- [Remains effective after exposure to rain or sunlight]

- [Fragrance free]
- [Contains the same active ingredients imidacloprid, pyriproxyfen and permethrin found in [Bayer] K9 Advantix II].
- [Contains the [same] active ingredients [found] [used] in [Bayer] K9 Advantix II]
- [T2.200 for Dogs is not manufactured by or distributed by Bayer Health Care LLC]
- [K9 Advantix II is a registered trademark of Bayer Health Care LLC]
- [Contains imidacloprid, pyriproxyfen and permethrin, the same active ingredients used in Bayer K9 Advantix II]
- [Compare to Bayer K9 Advantix II; Contains the same active ingredients as Bayer K9 Advantix II]
- [T2.200 is not manufactured by or distributed by Bayer Health Care LLC. K9 Advantix II is a registered trademark of Bayer HealthCare LLC]
- [3 Pack [3 Applicators][3 Months' Supply][3 Doses][3 Pipettes]]
- [4 Pack [4 Applicators][4 Months' Supply][4 Doses][4 Pipettes]]
- [6 Pack [6 Applicators][6 Months' Supply][6 Doses][6 Pipettes]]
- [8 Pack [8 Applicators][8 Months' Supply][8 Doses][8 Pipettes]]
- [12 Pack [12 Applicators][12 Months' Supply][12 Doses][12 Pipettes]]
- [3 Applications [Doses][Pipettes]]
- [4 Applications [Doses][Pipettes]]
- [6 Applications [Doses][Pipettes]]
- [8 Applications [Doses][Pipettes]]
- [12 Applications [Doses][Pipettes]]
- [Buy [3,4,6,8,] doses, get [1,2,3,4] free]
- [Small Dog [5-10 lbs.]]
- [Medium Dog [11-20 lbs.]]
- [Large Dog [21-55 lbs.]]
- [Ex Large Dog [Over 55 lbs.]]
- [Illustration of flea life cycle] [halts life cycle of fleas]
- [Illustration of tick life cycle] [halts life cycle of ticks]
- [Illustration of louse life cycle] [halts life cycle of lice]
- [Illustration of chewing lice life cycle] [halts life cycle of chewing lice]
- [Illustration of adult fleas] [kills [and repels] adult fleas]
- [Illustration of flea eggs] [stops hatching of flea eggs[in the environment]]
- [Illustration of flea larvae] [stops development of flea larvae[in the environment]]
- [Illustration of chewing lice] [kills chewing lice]
- [Illustration of tick] [kills[and repels] ticks]
- [Illustration of flea] [kills fleas]
- [Illustration of louse] [kills lice]
- [Illustration of mosquito] [kills[and repels] mosquitos[and biting flies]]
- [Illustration of biting fly [kills [and repels] biting flies]
- [5-way protection] 'Note to reviewer: To be associated with the 5 parasite illustrations.'
- [Picture or illustration of a dog or puppy of appropriate weight class]
- [Picture or illustration of the T2.200 logo]
- [Picture or illustration of the primary package, applicator tubes, pipettes]

(TEXT FOR REMINDER STICKERS)
NOTE TO REVIEWER: This entire section on reminder stickers is optional

[Optional marketing claims]

[Picture of Dog or Puppy 7 weeks or older]
[Picture of flea] [kills fleas]
[Picture of tick] [kills [and repels]ticks]
[Picture of chewing lice] [kills lice]
[Picture of mosquitoes] [kills [and repels]mosquitoes[and biting flies]]
[Long-lasting]
[Does not wash off]
[For monthly control of fleas, ticks, [biting flies], [chewing lice], mosquitoes]
[Optional Bar Code]

T2.200 for Dogs

The first time you treat your dog, place the First (Application) Sticker on your calendar. Apply Stickers [2 and 3] [2, 3, 4] [2 through 6] [2 through 8]to the calendar [30 and 60 days] [monthly] [30, 60, and 90 days] [30, 60, 90, 120, and 150 days] [30, 60, 90, 120, 150, 180, and 210 days] [at the end of each 30 day period] after the first [application][dose] to remind you it's time to reapply T2.200 for Dogs.

First Application [Dose][Sticker]: [Apply] T2.200 for Dogs
Month 2 [Sticker]: [Apply] T2.200 for Dogs
Month 3 [Sticker]: [Apply] T2.200 for Dogs
[Month 4 [Sticker]: [Apply] T2.200 for Dogs]
[Month 5 [Sticker]: [Apply] T2.200 for Dogs]
[Month 6 [Sticker]: [Apply] T2.200 for Dogs]
[Month 7 [Sticker]: [Apply] T2.200 for Dogs]
[Month 8 [Sticker]: [Apply] T2.200 for Dogs]

Do Not Use on Cats 

For Customer Service please call 1-8xx-xxx-xxxx.

CAP IM Supply, Inc.
303 Perimeter Center North, Suite 300
Atlanta, GA 30346

[Optional bar code]

Fertich, Elizabeth

From: Fertich, Elizabeth
Sent: Monday, September 19, 2016 3:07 PM
To: 'Richard L. Conn'
Cc: IVB1; John Tatum
Subject: RE: 91384-G (T2.200 for Dogs) Revised Data Matrix and Method of Support Forms

Hi Richard,
Thanks for sending the changes. I submitted everything to the PM for final review.
Kind regards,
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Richard L. Conn [mailto:richard@connsmith.com]
Sent: Monday, September 19, 2016 2:30 PM
To: Fertich, Elizabeth <fertich.elizabeth@epa.gov>
Cc: IVB1 <IVB1@epa.gov>; John Tatum <John.Tatum@CAPSupplyInc.com>
Subject: Re: 91384-G (T2.200 for Dogs) Revised Data Matrix and Method of Support Forms

Hi Beth,
CAP IM Supply has decided to provide the specific website, and actually has two optional websites now listed at the bottom of page 20. A "NOTE TO REVIEWER" sentence prefaces the two websites to indicate that these websites are currently under construction, but will go live before use on any packaging being released for shipment. I have attached a track changes version of the label dated September 19 to show the revisions on page 20 compared to what I provided to you September 15. A clean version of that label with the file name "091384-xxxxx.20160919.T2.200 for Dogs.pdf" is also attached for your use in accepting the label.

We will appreciate your continued processing and we will be available to answer any other last minute questions.

Best regards,
Richard

On 9/19/2016 11:15 AM, Fertich, Elizabeth wrote:

> Hi Richard,
> I have one minor comment on the revised label. On page 21, please remove the reference to the website or provide the specific website that will be included on the final label. Otherwise, I think your changes look good. I'll submit to the PM for final review today.
> Thanks,
> Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Fertich, Elizabeth
Sent: Thursday, September 15, 2016 2:24 PM
To: 'Richard L. Conn' <richard@connsmith.com>
Cc: IVB1 <IVB1@epa.gov>; John Tatum <John.Tatum@CAPSupplyInc.com>
Subject: RE: 91384-G (T2.200 for Dogs) Revised Data Matrix and Method of Support Forms

Hi Richard,
Thanks for providing the revised label. I'll let you know if I have any additional questions or comments.
Kind regards,
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Richard L. Conn [mailto:richard@connsmith.com]
Sent: Thursday, September 15, 2016 11:24 AM
To: Fertich, Elizabeth <fertich.elizabeth@epa.gov>
Cc: IVB1 <IVB1@epa.gov>; John Tatum <John.Tatum@CAPSupplyInc.com>
Subject: Re: 91384-G (T2.200 for Dogs) Revised Data Matrix and Method of Support Forms

Beth,
CAP IM Supply, Inc. has agreed to all of the label revisions you had identified on the track changes label you sent yesterday afternoon, and the two attached files reflect those changes. In addition to the label revisions you identified yesterday, CAP IM Supply noticed five minor items it had missed earlier when carefully checking the label late yesterday, so each of those five minor items we missed earlier are highlighted in yellow in the attached file "T2.200 revised label Sept 15 2016 track changes plus yellow highlighting.pdf". We believe you will be able to concur with those five yellow highlighted revisions. All of the track changes revisions that you identified yesterday are indicated in red color in that file.

We have attached "091384-xxxxx.20160915.T2.200 for Dogs.pdf" which is the final clean version of the label that can be used for your acceptance stamp.

Please let me know if you have any questions.

Best regards,
Richard

On 9/14/2016 2:44 PM, Fertich, Elizabeth wrote:

Richard,
Please see the attached letter and label annotated with my comments. Please review and let me know if you have any questions.
Kind regards,
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Fertich, Elizabeth
Sent: Tuesday, September 13, 2016 1:18 PM
To: 'Richard L. Conn' <richard@connsmith.com>
Cc: IVB1 <IVB1@epa.gov>; John Tatum <John.Tatum@CAPSupplyInc.com>
Subject: RE: 91384-G (T2.200 for Dogs) Revised Data Matrix and Method of Support Forms

Richard,
Thanks for sending the electronic labels. I've sent my comments to the PM for review and will send the document to you later today or tomorrow.
Kind regards,
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Richard L. Conn [mailto:richard@connsmith.com]
Sent: Monday, September 12, 2016 5:29 PM
To: Fertich, Elizabeth <fertich.elizabeth@epa.gov>
Cc: IVB1 <IVB1@epa.gov>; John Tatum <John.Tatum@CAPSupplyInc.com>
Subject: Re: 91384-G (T2.200 for Dogs) Revised Data Matrix and Method of Support Forms

Beth,
The attached labeling goes back to the original packaging that was in our initial application dated December 3, 2015 that I delivered to Document Processing December 7, 2015. Both the clean electronic version of our proposed label, now dated September 12, 2016 and the track changes version (changes compared to the labeling that was in the December 2015 application) are attached.

We will be ready to quickly process the revisions needed to give you a good clean version of the label to complete your processing.

Fertich, Elizabeth

From:	Richard L. Conn <richard@connsmith.com>
Sent:	Monday, September 12, 2016 5:29 PM
To:	Fertich, Elizabeth
Cc:	IVB1; John Tatum
Subject:	Re: 91384-G (T2.200 for Dogs) Revised Data Matrix and Method of Support Forms
Attachments:	091384-xxxxx.20160912.T2.200 for Dogs--showing track changes.pdf; 091384-xxxxx.20160912.T2.200 for Dogs.pdf
Follow Up Flag:	Follow up
Flag Status:	Completed

Beth,
The attached labeling goes back to the original packaging that was in our initial application dated December 3, 2015 that I delivered to Document Processing December 7, 2015. Both the clean electronic version of our proposed label, now dated September 12, 2016 and the track changes version (changes compared to the labeling that was in the December 2015 application) are attached.

We will be ready to quickly process the revisions needed to give you a good clean version of the label to complete your processing.

Best regards,
Richard

On 9/12/2016 4:06 PM, Fertich, Elizabeth wrote:

> Richard,
> Thanks for the update. I've finished my review and will be ready to send the comments shortly after I receive the electronic copy.
> Kind regards,
> Beth
>
> Elizabeth Fertich
> US Environmental Protection Agency
> Office of Pesticide Programs
> Registration Division (7505P)
> Invertebrate and Vertebrate Branch 1 (IVB1)
> fertich.elizabeth@epa.gov
> 703-347-8560
>
> **From:** Richard L. Conn [mailto:richard@connsmith.com]
> **Sent:** Monday, September 12, 2016 2:50 PM
> **To:** Fertich, Elizabeth <fertich.elizabeth@epa.gov>
> **Subject:** Re: 91384-G (T2.200 for Dogs) Revised Data Matrix and Method of Support Forms
>
> Beth,
> I am working on the label for you and will get it into your hands ASAP (no later than first thing Tuesday morning, but hopefully late this afternoon).

Best regards,
Richard

On 9/12/2016 11:44 AM, Fertich, Elizabeth wrote:

> Richard,
> I'm working on your label now. Please send me an electronic copy of the most recent version of the label. I have a hard copy of one dated 6/13 that was submitted with the request to use different CRP packaging. I assume this is invalid as you are now using the originally proposed packaging. Please confirm and submit a copy of the correct version of the label.
> Thanks,
> Beth
>
> Elizabeth Fertich
> US Environmental Protection Agency
> Office of Pesticide Programs
> Registration Division (7505P)
> Invertebrate and Vertebrate Branch 1 (IVB1)
> fertich.elizabeth@epa.gov
> 703-347-8560
>
> **From:** Richard L. Conn [mailto:richard@connsmith.com]
> **Sent:** Wednesday, September 07, 2016 10:38 AM
> **To:** Fertich, Elizabeth <fertich.elizabeth@epa.gov>
> **Cc:** Bacon, Laura <Bacon.Laura@epa.gov>; John Tatum <John.Tatum@CAPSupplyInc.com>
> **Subject:** 91384-G (T2.200 for Dogs) Revised Data Matrix and Method of Support Forms
>
> Hi Beth,
> On behalf of CAP IM Supply, Inc. I am transmitting to you in this email the revised data matrix (EPA Form 8570-35) and the revised Certification with Respect to Citation of Data (EPA Form 8570-34) for EPA File Symbol 91384-G, T2.200 for Dogs. With these revised forms, for the efficacy data requirement only, CAP IM Supply has switched to the cite-all method of support, and has retained the selective method of support for all other data requirements. CAP IM Supply has sent the required Offer to Pay letters to each of the other data submitters listed as having submitted efficacy data on the most recent Data Submitters List that EPA published June 30, 2016 for each of the three active ingredients present in T2.200 for Dogs (imidacloprid, permethrin, and pyriproxyfen).
>
> It is our understanding from the conversation I had with you on September 1 that with our submission of the revised data matrix to reflect our use of the cite-all method for efficacy data, the current PRIA due date of September 28, 2016 will remain in place. We also understand from that discussion with me that there is an acceptable product chemistry review from June 2016 that will be forwarded to us, as well as an acceptable acute toxicology review that was recently completed that will also be forwarded to us. We hereby are committing that we will respond in a timely manner upon receipt of any label revision comments from you as you work through that step of these final stages of processing of the EPA File Symbol 91384-G application.

Please let us know when any questions and comments arise during these final review stages for our T2.200 for Dogs product.

Best regards,
Richard

--
Richard L. Conn, President, Conn & Smith, Inc.
6713 Catskill Rd, Lorton VA 22079-1113, USA
Phone: (703) 339-4199
http://www.connsmith.com

--
Richard L. Conn, President, Conn & Smith, Inc.
6713 Catskill Rd, Lorton VA 22079-1113, USA
Phone: (703) 339-4199
http://www.connsmith.com

DATA MATRIX

Date: **September 7, 2016**	EPA Reg No./File Symbol: **91384-G**	Page 1 of 5
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc.** **303 Perimeter Center North Ste 300** **Atlanta, GA 30346**	Product: **T2.200 for Dogs**	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
	SEE SUBSEQUENT PAGES				

Signature:	Name and Title:	Date:
John A. Tatum III/RLC	John A. Tatum III, Chief Operating Officer	9-7-16

Produced from EPA Form 8570-35 (9-97)

Agency Internal Use Copy

DATA MATRIX

Date: **September 7, 2016**	EPA Reg No./File Symbol: **91384-G**	Page 2 of 5
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Treatments to control pests of humans and pets	CITE-ALL	Under the cite-all method of support for efficacy data, CAP IM Supply, Inc. has made offers to pay to the data submitters listed in the attached "Efficacy Data Submitters Based on the June 30, 2016 Data Submitters List".		
830.1550	Product identity and composition	49799701	91639	PER	
830.1600	Description of materials used to produce the product	49799701	91639	PER	
830.1650	Description of formulation process	49799701	91639	PER	
830.1670	Discussion of formation of impurities	49799701	91639	PER	
830.1750	Certified limits	49799701	91639	PER	
830.1800	Enforcement analytical method	49799701	91639	PER	
830.6302	Color	49788714	91639	PER	
830.6303	Physical state	49788714	91639	PER	
830.6304	Odor	49788714	91639	PER	
830.6314	Oxidation/reduction: chemical incompatibility				Not applicable -- product does not contain an oxidizing or reducing agent
830.6315	Flammability	49788714	91639	PER	
830.6316	Explodability				Not applicable -- product not potentially explosive

DATA MATRIX

Date: **September 7, 2016**	EPA Reg No./File Symbol: **91384-G**	Page 3 of 5
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
830.6317	Storage stability	49788714	91639	PER	
830.6319	Miscibility				Not applicable -- not an emulsifiable liquied to be diluted with petroleum solvent
830.6320	Corrosion characteristics	49788714	91639	PER	
830.6321	Dielectric breakdown voltage				Not applicable -- not to be used around electrical equipment
830.7000	pH	49788714	91639	PER	
830.7100	Viscosity	49788714	91639	PER	
830.7300	Density/relative density/bulk density	49788714	91639	PER	
830.7520	Particle size, fiber length, and diameter distribution				Not applicable -- not a water insoluble substance or fibrous substance
870.1100	Acute oral toxicity	49788715	91639	PER	B-01983 - Acute oral toxicity – Acute toxic class method
870.1200	Acute dermal toxicity	49788716	91639	PER	B-01984 - Acute dermal toxicity
870.1300	Acute inhalation toxicity				Waiver requested due to product being liquid with low volatility and maximum 4 mL as a single dose to skin of dogs

DATA MATRIX

Date: **September 7, 2016**	EPA Reg No./File Symbol: **91384-G**	Page 4 of 5
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.2400	Acute eye irritation	49788717	91639	PER	N-01986 - Non-GLP Acute Eye Irritation / Corrosion
870.2400	Acute eye irritation	49788718	91639	PER	B-01981 - Acute eye irritation / corrosion
870.2500	Acute dermal irritation	49788719	91639	PER	B-01980 - Acute dermal irritation
870.2600	Skin sensitization	49788720	91639	PER	E-01982 - Skin sensitization – Local lymph node assay
870.7200	Companion animal safety	49788721 and 49866901	91639	PER	CV-15-154 - Target Animal Safety Adults (>6 months old)
870.7200	Companion animal safety	49788722 and 49866902	91639	PER	CV-15-155 - Target Animal Safety Puppies (<7 weeks old)
157.20	Child-resistant packaging testing	49649301	74720	PER	Report KVS-201501
157.20	Child-resistant packaging testing	49649305	74720	PER	Report KVS-201505
157.20	Child-resistant packaging testing	49649308	74720	PER	Report KVS-201508
157.20	Child-resistant packaging testing	49649309	74720	PER	Report KVS-201509
157.20	Child-resistant packaging testing	49649310	74720	PER	Report KVS-201510
157.20	Child-resistant packaging testing	49649313	74720	PER	Report KVS-201513
157.20	Child-resistant packaging testing	49681401	74720	PER	Report KVS-201514
157.20	Child-resistant packaging testing	49681402	74720	PER	Report KVS-201515

DATA MATRIX					
Date: **September 7, 2016**		EPA Reg No./File Symbol: **91384-G**			Page 5 of 5
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**		Product: **T2.200 for Dogs**			
Ingredient: **permethrin (CAS No. 52645-53-1), pyriproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**					
Guideline Reference Number	**Guideline Study Name**	**MRID Number**	**Submitter**	**Status**	**Note**
157.20	Child-resistant packaging testing	49681403	74720	PER	Report KVS-201516
157.20	Child-resistant packaging testing	49719401	74720	PER	Report KVS-201517
157.20	Child-resistant packaging testing	49719402	74720	PER	Report KVS-201518
157.20	Child-resistant packaging testing	49719403	74720	PER	Report KVS-201521

Efficacy Data Submitters
Based on the June 30, 2016 Data Submitters List
Who were Sent Offer-To-Pay Letters for EPA File Symbol 91384-G

EPA Company Number	Company Name	129099 Imidacloprid	109701 Permethrin	129032 Pyriproxyfen
59	COOPERS ANIMAL HEALTH INC DIRECTOR OF REGULATORY AFFAIRS 421 EAST HAWLEY ST MUNDELEIN,IL 60060		X	
100	SYNGENTA CROP PROTECTION, LLC P.O. BOX 18300 410 SWING ROAD GREENSBORO,NC 27419	X	X	
228	NUFARM AMERICAS, INC. 4020 AERIAL CENTER PKWY., STE. 101 MORRISVILLE,NC 27560	X		
239	THE SCOTTS COMPANY D/B/A THE ORTHO GROUP 14111 SCOTTSLAWN ROAD MARYSVILLE,OH 43041		X	X
264	BAYER CROPSCIENCE LP P.O. BOX 12014 2 T.W. ALEXANDER DRIVE RESEARCH TRIANGLE PARK,NC 27709	X		
270	FARNAM COMPANIES, INC. 1501 E. WOODFIELD ROAD., SUITE 200 WEST SCHAUMBURG,IL 60173		X	
279	FMC CORPORATION 2929 WALNUT STREET PHILADELPHIA,PA 19104		X	X
352	E. I. DU PONT DE NEMOURS AND COMPANY (S300/419) ATTN: MANAGER, US REGISTRATION, DUPONT CHESTNUT RUN PLAZA, 974 CENTRE ROAD PO BOX 2915 WILMINGTON,DE 19805	X		
400	MACDERMID AGRICULTURAL SOLUTIONS, INC. ATTN: REGISTRATION DEPARTMENT 245 FREIGHT STREET WATERBURY,CT 06702		X	
432	BAYER ENVIRONMENTAL SCIENCE A DIVISION OF BAYER CROPSCIENCE LP P.O. BOX 12014 2 T. W. ALEXANDER DRIVE RESEARCH TRIANGLE PARK,NC 27709	X	X	
478	REALEX DIV OF UNITED INDUSTRIES CORP P.O. BOX 142642 ST LOUIS,MO 63114		X	
499	BASF CORPORATION P.O. BOX 13528 26 DAVIS DRIVE RESEARCH TRIANGLE PARK,NC 27709		X	X
524	MONSANTO COMPANY MONSANTO COMPANY 1300 I STREET, NW, SUITE 450 EAST WASHINGTON,DC 20005	X		
769	VALUE GARDENS SUPPLY, LLC D/B/A VALUE GARDEN SUPPLY 640 GRISWOLD STREET, SUITE 200 NORTHVILLE,MI 48167		X	
773	INTERVET, INC D/B/A MERCK ANIMAL HEALTH 2 GIRALDA FARMS, MAH-3100 MADISON,NJ 07941		X	

Efficacy Data Submitters
Based on the June 30, 2016 Data Submitters List
Who were Sent Offer-To-Pay Letters for EPA File Symbol 91384-G

EPA Company Number	Company Name	129099 Imidacloprid	109701 Permethrin	129032 Pyriproxyfen
1021	MCLAUGHLIN GORMLEY KING COMPANY D/B/A MGK 8810 TENTH AVE NORTH MINNEAPOLIS,MN 55427	X	X	X
1022	IBC MANUFACTURING CO 416 E BROOKS ROAD MEMPHIS, TN 38109		X	
1543	W.F. YOUNG, INC. 302 BENTON DRIVE EAST LONGMEADOW,MA 01028		X	
2382	VIRBAC AH, INC. 3200 MEACHAM BOULEVARD FORT WORTH,TX 76137		X	X
2517	SERGEANT'S PET CARE PRODUCTS, INC. P.O. BOX 540399 OMAHA,NE 68154		X	X
2596	THE HARTZ MOUNTAIN CORPORATION 400 PLAZA DRIVE SECAUCUS,NJ 07094	X	X	X
2724	WELLMARK INTERNATIONAL 1501 E. WOODFIELD ROAD, SUITE 200 WEST SCHAUMBURG,IL 60173		X	
2781	HAPPY JACK INC. TECHNOLOGY SCIENCES GROUP INC. 1150 18TH STREET, N.W., SUITE 1000 WASHINGTON,DC 20036		X	
2791	MILLER W C CHEM CO 3314 HOUSTON AVE HOUSTON,TX 77009		X	
3008	KOPPERS PERFORMANCE CHEMICALS, INC. 1016 EVEREE INN ROAD GRIFFIN,GA 30224	X		
3125	BAYER CORP AGRICULTURE DIVISION P.O. BOX 4913 8400 HAWTHORN RD KANSAS CITY,MO 64120	X		
4787	CHEMINOVA A/S FMC CORPORATION 1735 MARKET STREET, ROOM 1971 PHILADELPHIA,PA 19103		X	
4822	S.C. JOHNSON & SON INC. 1525 HOWE STREET RACINE,WI 53403		X	
5481	AMVAC CHEMICAL CORPORATION 4695 MACARTHUR COURT, SUITE 1200 NEWPORT BEACH,CA 92660		X	
6218	SUMMIT CHEMICAL CO. SUMMIT RESPONSIBLE SOLUTIONS 8322 SHARON DRIVE FREDERICK,MD 21704		X	
6959	CESSCO INC 3609A RIVER RD JOHNS ISLAND,SC 29455		X	
7946	J. J. MAUGET CO. SCIREG, INC. 12733 DIRECTOR'S LOOP WOODBRIDGE,VA 22192	X	X	

Efficacy Data Submitters
Based on the June 30, 2016 Data Submitters List
Who were Sent Offer-To-Pay Letters for EPA File Symbol 91384-G

EPA Company Number	Company Name	129099 Imidacloprid	109701 Permethrin	129032 Pyriproxyfen
9688	CHEMSICO A DIVISION OF UNITED INDUSTRIES CORP. P.O. BOX 142642 ST LOUIS,MO 63114		X	X
10182	SYNGENTA CROP PROTECTION 410 SWING ROAD GREENSBORO,NC 27409		X	
10308	SUMITOMO CHEMICAL COMPANY, LTD. ENVIRONMENTAL HEALTH DIVISION 1150 18TH ST. NW, SUITE 1000 WASHINGTON,DC 20036			X
11556	BAYER HEALTHCARE LLC ANIMAL HEALTH DIVISION P.O. BOX 390 SHAWNEE MISSION,KS 66201	X	X	X
11930	GIL MFG INC. IPM RESOURCES, LLC 4032 CROCKERS LAKE BLVD., STE. 818 SARASOTA,FL 34238		X	
14663	I2LRESEARCH USA, INC. 1330 DILLON HEIGHTS AVE BALTIMORE,MD 21228		X	
20954	SANDOZ AGRO INC 1300 EAST TOUHY AVE DES PLAINES,IL 60018		X	
33657	MITSUI CHEMICALS, INC. LANDIS INTERNATIONAL, INC. P.O. BOX 5126 VALDOSTA,GA 31603	X	X	
39039	Y-TEX CORPORATION 1825 BIG HORN AVENUE CODY,WY 82414		X	
39967	LANXESS CORPORATION 111 RIDC PARK WEST DRIVE PITTSBURGH,PA 15275	X		
40086	CHATTEM, INC. ATTN: JENNIFER PALMER, MGR REGULATORY 1715 WEST 38TH ST CHATTANOOGA,TN 37409			X
43419	AEROXON INC. 2125 CENTER AVE., SUITE 507 FORT LEE,NJ 07024	X		
45385	CTX-CENOL, INC. 1393 EAST HIGHLAND RD. TWINSBURG,OH 44087		X	
46515	CELEX, DIVISION OF UNITED INDUSTRIES C P.O. BOX 142642 ST LOUIS,MO 63114		X	
50404	COULSTON PRODUCTS INC SCIENTIFIC COORDINATION, INC. 4629 CHERRY VALLEY DRIVE ROCKVILLE,MD 20853		X	
53263	BASF CORPORATION ATTENTION: JANET CERRA 100 PARK AVENUE FLORHAM PARK,NJ 07932		X	

Efficacy Data Submitters
Based on the June 30, 2016 Data Submitters List
Who were Sent Offer-To-Pay Letters for EPA File Symbol 91384-G

EPA Company Number	Company Name	129099 Imidacloprid	109701 Permethrin	129032 Pyriproxyfen
53883	CONTROL SOLUTIONS, INC. 5903 GENOA-RED BLUFF ROAD PASADENA,TX 77507	X	X	X
54022	VIRBAC RICHARD A. HAMER ASSOCIATES, REGULATOR P.O. BOX 16598 FORT WORTH,TX 76162		X	
59639	VALENT U.S.A. CORPORATION 1600 RIVIERA AVENUE, SUITE 200 WALNUT CREEK,CA 94596	X		
63823	MANAGEMENT CONTRACT SERVICES, INC. P.O. BOX 5209 VALDOSTA,GA 31603			X
64405	NISUS CORPORATION ATTN: REGULATORY AFFAIRS 100 NISUS DRIVE ROCKFORD,TN 37853		X	
64977	PYRETHROID WORKING GROUP C/O LANDIS INTERNATIONAL, INC. P.O. BOX 5126 VALDOSTA,GA 31603		X	
65331	MERIAL, INC. HEAD, REGULATORY AFFAIRS LIFECYCLE MAN 3239 SATELLITE BLVD, BLDG 500, OFFICE 113 DULUTH,GA 30096		X	
68086	SYNERGY LABS 3201 SW 42ND STREET FORT LAUDERDALE,FL 33312		X	
68467	MYCOGEN SEEDS C/O DOW AGROSCIENCES LLC 9330 ZIONSVILLE ROAD INDIANAPOLIS,IN 46268	X		
68543	BENGAL PRODUCTS INC 13739 AIRLINE HWY BATON ROUGE,LA 70817		X	
69117	ARBORSYSTEMS, INC. D/B/A ARBOR SYSTEMS 8203 WEST 20TH STREET, SUITE A GREELEY,CO 80634	X		
69332	PET LOGIC, L.L.C. P.O. BOX 540224 OMAHA,NE 68130	X		X
71720	RIAP CHEMICAL FACTORY ALEXANDRA C. MELNYK 801 BOVEE LANE BOVEE,OH 43065		X	
72155	BAYER ADVANCED A BUSINESS UNIT OF BAYER CROPSCIENCE LP P.O. BOX 12014 2 T.W. ALEXANDER DRIVE RESEARCH TRIANGLE PARK,NC 27709	X	X	
72500	SCIMETRICS, LTD. CORPORATION P.O. BOX 1045 WELLINGTON,CO 80549	X		
72616	ZELAM LTD. ARCH WOOD PROTECTION INC. 3941 BONSAL ROAD CONLEY,GA 30288	X		

Efficacy Data Submitters
Based on the June 30, 2016 Data Submitters List
Who were Sent Offer-To-Pay Letters for EPA File Symbol 91384-G

EPA Company Number	Company Name	129099 Imidacloprid	109701 Permethrin	129032 Pyriproxyfen
72969	STAR HORSE PRODUCTS INC. TECHNOLOGY SCIENCES GROUP, INC. 712 FIFTH STREET, SUITE A DAVIS,CA 94596		X	
73049	VALENT BIOSCIENCES CORPORATION 870 TECHNOLOGY WAY LIBERTYVILLE,IL 60048		X	
73079	ROCKWELL LABS LTD D/B/A MAGGIE'S FARM LTD 1257 BEDFORD AVENUE NORTH KANSAS CITY,MO 64116	X		
73617	PRO PRODUCTS 36 SPLIT ROCK ROAD MAHOPAC,NY 10541		X	
73766	INNOVATIVE PEST CONTROL PRODUCTS P.O. BOX 880216 BOCA RATON,FL 33488	X		
74578	ARBORJET, INC. DELTA ANALYTICAL CORPORATION 12510 PROSPERITY DRIVE, SUITE 160 SILVER SPRING,MD 20904	X		
74843	INSECT SHIELD, LLC 814 W. MARKET STREET GREENSBORO,NC 27401		X	
75257	STAR BUSINESS PRODUCTS INC. PYXIS REGULATORY CONSULTING, INC. 4110 136TH STREET CT. NW GIG HARBOR,WA 98332		X	X
75844	ANDREW M. MARTIN CO., NV INC. PYXIS REGULATORY CONSULTING, INC. 4110 136TH STREET CT NW GIG HARBOR,WA 98332		X	X
80203	STARENSIER, INC. P.O. BOX 737 12 KENT WAY, SUITE 201 BYFIELD,MA 01922		X	
81041	BIKEL INTERNATIONAL, INC. HEALTH & ENVIRONMENTAL HORIZONS, LTD. 2851 SOUTHHAVEN RD ANNAPOLIS,MD 21401		X	
82108	EASTERN CHEMICAL, LLC C/O BUZZ OFF INSECT SHIELD, LLC P.O. BOX 10129 GREENSBORO,NC 27404		X	
82123	ALLERGY TECHNOLOGIES, LLC PRODUCT & REGULATORY ASSOCIATES, LLC P.O. BOX 1683 VOORHEES,NJ 08043		X	
82392	PINEBELT PROCESSING, INC. HENRY JACOBY REGULATORY CONSULTANT 6709 ILEX COURT NEW MARKET,MD 21774		X	
82669	HOMS LLC P.O. BOX 1887 193 LORAX LANE PITTSBORO,NC 27312		X	
83122	GARNIK INDUSTRIES, LLC 261 5TH AVENUE, SUITE 2001 NEW YORK,NY 10016		X	

Efficacy Data Submitters
Based on the June 30, 2016 Data Submitters List
Who were Sent Offer-To-Pay Letters for EPA File Symbol 91384-G

EPA Company Number	Company Name	129099 Imidacloprid	109701 Permethrin	129032 Pyriproxyfen
83399	CEVA ANIMAL HEALTH, LLC 8735 ROSEHILL ROAD LENEXA,KS 66215	X	X	X
83588	INTERNATIONAL TEXTILE GROUP, INC. ATTN: MIKE GARLICK 804 GREEN VALLEY ROAD, SUITE 300 GREENSBORO,NC 27408		X	
83923	ENSYSTEX IV, INC PYXIS REGULATORY CONSULTING, INC. 4110 136TH STREET GIG HARBOR,WA 98332	X		
83997	VIANCE, LLC 8001 IBM DRIVE CHARLOTTE,NC 28262	X		
85354	ALPHA SCENTS, INC TECHNOLOGY SCIENCES GROUP INC. 1150 18TH STREET, NW, SUITE 1000 WASHINGTON,DC 20036	X		
85391	8-S INVESTMENT AND MANAGEMENT INC. H.R. MCLANE, INC 7210 RED RD., SUITE 206A MIAMI, ,FL 33143			X
86468	BRITTANY GLOBAL TECHNOLOGIES CORP. PRODUCT & REGULATORY ASSOCIATES, LLC 8595 COLLIER BLVD., SUITE 107-51 NAPLES,FL 34114		X	
88665	TRITON SYSTEMS, INC. SCIREG, INC. 12733 DIRECTOR'S LOOP WOODBRIDGE,VA 22192		X	
89609	TRURX, LLC 500 E. SHORE DRIVE, SUITE 130 EAGLE,ID 83616		X	
91384	CAP IM SUPPLY, INC. 303 PERIMETER CENTER NORTH SUITE 300 ATLANTA ,GA 30346	X	X	X
91605	FLORIDA INSECT CONTROL GROUP LLC LANDIS INTERNATIONAL P.O. BOX 5126 VALDOSTA ,GA 31603		X	X

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 1.25 hours per response for registration and 0.25 hours per response for reregistration and special review activities, including time for reading the instructions and completing the necessary forms. Send comments regarding burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the completed form to this address.

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number	EPA Registration Number/File Symbol
CAP IM Supply, Inc., 303 Perimeter Center North Ste 300, Atlanta, GA 30346 (801) 512-7543	91384-G
Active Ingredient(s) and/or representative test compound(s): permethrin, imidacloprid, pyriproxyfen	Date: 9-7-16
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158): indoor nonfood	Product Name: T2.200 for Dogs

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I- METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

☒ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements]

☒ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is *indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or* substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses .

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (1) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
John A. Tatum III/alc	9-7-16	John A. Tatum III, Chief Operating Officer

EPA Form 8570-34 (9-97) Electronic and Paper versions available. Submit only Paper version.

Fertich, Elizabeth

From:	Richard L. Conn <richard@connsmith.com>
Sent:	Wednesday, September 07, 2016 10:38 AM
To:	Fertich, Elizabeth
Cc:	Bacon, Laura; John Tatum
Subject:	91384-G (T2.200 for Dogs) Revised Data Matrix and Method of Support Forms
Attachments:	91384-G T2.200 for Dogs revised 8570-34 signed Sept 7 2016.pdf; T2.200 for Dogs 8570-35 signed agency version rev 9-7-16.pdf; T2.200 for Dogs 8570-35 signed public version rev 9-7-16.pdf
Follow Up Flag:	Follow up
Flag Status:	Flagged

Hi Beth,
On behalf of CAP IM Supply, Inc. I am transmitting to you in this email the revised data matrix (EPA Form 8570-35) and the revised Certification with Respect to Citation of Data (EPA Form 8570-34) for EPA File Symbol 91384-G, T2.200 for Dogs. With these revised forms, for the efficacy data requirement only, CAP IM Supply has switched to the cite-all method of support, and has retained the selective method of support for all other data requirements. CAP IM Supply has sent the required Offer to Pay letters to each of the other data submitters listed as having submitted efficacy data on the most recent Data Submitters List that EPA published June 30, 2016 for each of the three active ingredients present in T2.200 for Dogs (imidacloprid, permethrin, and pyriproxyfen).

It is our understanding from the conversation I had with you on September 1 that with our submission of the revised data matrix to reflect our use of the cite-all method for efficacy data, the current PRIA due date of September 28, 2016 will remain in place. We also understand from that discussion with me that there is an acceptable product chemistry review from June 2016 that will be forwarded to us, as well as an acceptable acute toxicology review that was recently completed that will also be forwarded to us. We hereby are committing that we will respond in a timely manner upon receipt of any label revision comments from you as you work through that step of these final stages of processing of the EPA File Symbol 91384-G application.

Please let us know when any questions and comments arise during these final review stages for our T2.200 for Dogs product.

Best regards,
Richard

--
Richard L. Conn, President, Conn & Smith, Inc.
6713 Catskill Rd, Lorton VA 22079-1113, USA
Phone: (703) 339-4199
http://www.connsmith.com

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

To: Elizabeth Fertich

From: Tim Ciarlo, MS, Entomologist

Secondary Review: Pesticide Efficacy Review Committee

Date: August 30, 2016

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD (DER)

THIS DER CONTAINS CONFIDENTIAL BUSINESS INFORMATION

Note: MRIDs found to be **unacceptable** to support label claims should be removed from the data matrix.

DP barcode: 435335
Decision no.: 511951
Submission no: 990856
Action code: R315
Product Name: T2.200 for Dogs
EPA File Symbol: 91384-G
Formulation Type: Spot-On for Dogs
Ingredients statement from the label with PC codes included:

Permethrin	44%	PC: 109701
Imidacloprid	8.8%	PC: 129099
Pyriproxyfen	0.44%	PC: 129032

Application rate(s) of product and each active ingredient (lbs. or gallons/1000 square feet or per acre as appropriate; and g/m^2 or mg/cm^2 or mg/kg body weight as appropriate): The proposed label assigns 4 different sizes according to a dog's body weight. For 4-10 lb (1.81-4.54 kg) dogs, a 0.4 ml dose is indicated. For 11-20 lb (4.99-9.07 kg) dogs, a 1.0 ml dose is indicated. For 21-55 lb (9.53-24.95 kg) dogs, a 2.5 ml dose is indicated. For dogs over 55 lbs (24.95 kg), a 4.0 ml dose is indicated. Active ingredient doses are identified below. Ninety pounds was used as the upper end of the largest weight range, despite the label not giving an upper limit.

Body Weight Class	Amount of Product Applied	Active Ingredient Doses (mg/kg)*
4-10 lbs or 1.81-4.54 kg	0.4 ml (0.46 g)	Imidacloprid – 22.35 to 8.94 (at 10 lbs) Permethrin – 111.17 to 44.70 (at 10 lbs) Pyriproxyfen – 1.18 to 0.45 (at 10 lbs)
11-20 lbs or 4.99-9.07 kg	1.0 ml (1.152 g)	Imidacloprid – 20.31 to 11.17 (at 20 lbs) Permethrin – 101.58 to 55.86 (at 20 lbs) Pyriproxyfen – 1.06 to 0.56 (at 20 lbs)
21-55 lbs or 9.53-24.95 kg	2.5 ml (2.88 g)	Imidacloprid – 26.61 to 10.16 (at 55 lbs) Permethrin – 133.04 to 50.79 (at 55 lbs) Pyriproxyfen – 1.33 to 0.51 (at 55 lbs)

>55 lbs or >24.95 kg	4.0 ml (4.608)	Imidacloprid – 16.25 to 9.93 (at 90 lbs) Permethrin – 81.27 to 49.67 (at 90 lbs) Pyriproxyfen – 0.81 to 0.50 (at 90 lbs)

*Based on a product density of 1.152 g/ml and active ingredient concentrations listed above.

Imidacloprid dosages are: 8.94 mg/kg to 26.61 mg/kg
Permethrin dosages are: 44.70 mg/kg to 133.04 mg/kg
Pyriproxyfen dosages are: 0.45 mg/kg to 1.33 mg/kg

Use Patterns: Monthly spot-on insecticide for dogs, applied to the skin between the dog's shoulder blades. For dogs weighing 4-10 lbs and 11-20 lbs, apply product to one spot. For dogs weighing 21-55 lbs and over 55 lbs, apply product in 3 or 4 spots on the top of the back of the dog from the shoulder to the base of the tail.

I. Action Requested: The registrant submitted a rebuttal to a previous review (DP# 431031) and is requesting that the Agency reconsider the conclusions made therein.

II. Background: Data were submitted in an R315 application package to support efficacy claims for the proposed new product 91384-G. In the Agency's review (DP# 431031), it was determined that the doses used throughout were inappropriate and could not support that the product is efficacious for dogs at the upper end of each labeled weight range. The lowest labeled rate (dose) was not used. Instead, one of four doses was applied to each test animal according to the proposed weight range in which each animal fell. All efficacy claims were therefore determined to be unacceptable.

III. Registrant Rebuttal Points and EPA Response:

Rebuttal Point 1: [redacted]

Claimed confidential by submitter

[redacted]

EPA Response: The proposed product is not considered a me-too product; therefore, the submitted efficacy data were reviewed as they pertain to the proposed product. The registrant is free to cite existing efficacy data, but all newly submitted efficacy data are reviewed.

Rebuttal Point 2: [redacted]

EPA Response: The registrant is correct to note that OPPTS Guideline 810.3300 was published before the advent of pet spot-on products, and that there is consequently no reference to designing efficacy studies which can adequately assess them. While there are plans to update this Guideline with the latest industry advances, registrants are encouraged to submit a study protocol for Agency review before conducting the study itself if they feel that current Guidelines do not address certain types of studies. This ensures that a subsequent study is capable of producing the type of data which may support product registration from an efficacy standpoint. Without an Agency protocol review, the registrant is subject to the Agency's evaluation of the efficacy data generated within the context of proposed label claims. The 45/90 day screen only ensures that the materials submitted are complete. The

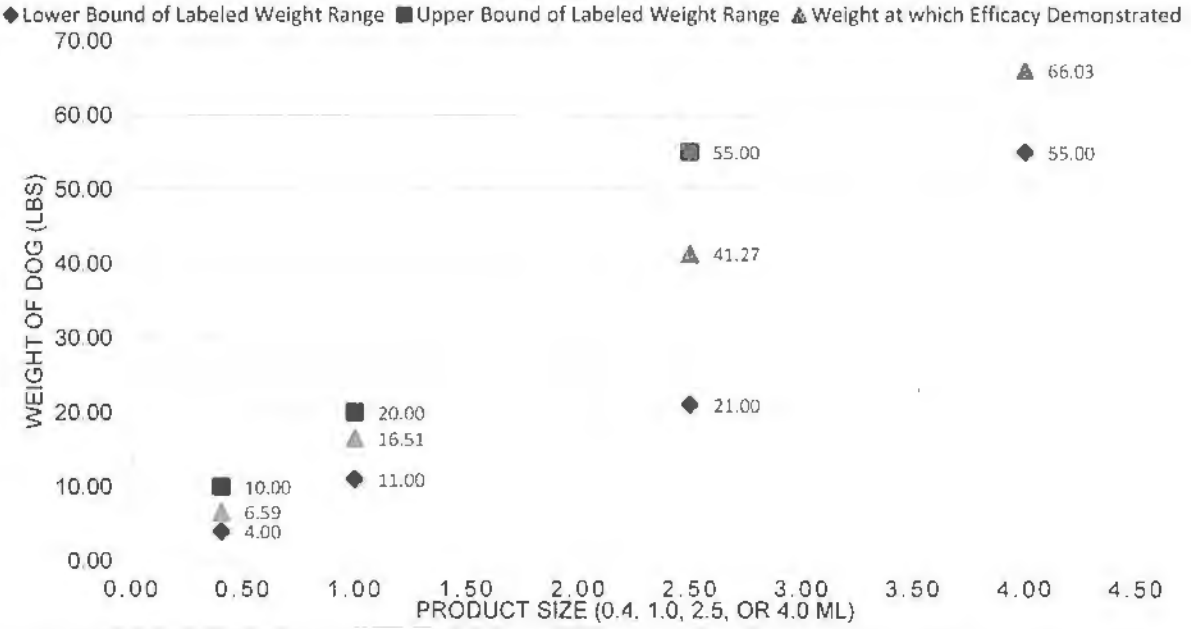
Claimed confidential by submitter

deficiencies identified in the Agency's review dated 7/27/2016 would only become apparent once the studies were formally reviewed.

For the Agency to make a determination that a product can be efficacious, **the lowest labeled rate** (dose, in the case of spot-on products) should be used in supporting efficacy studies, as this represents the most conservative rate that might be seen by a consumer. If failure of a product to work when used as directed were to occur, it would be most likely be at the lowest labeled rate. In this case, the proposed lowest labeled rates on the 91384-G label are 8.94 mg/kg imidacloprid, 44.70 mg/kg permethrin, and 0.45 mg/kg pyriproxyfen. However, the doses used throughout the efficacy studies submitted to support the proposed product were in all cases higher than the lowest labeled rates.

A titrated dose allows the lowest labeled rate to be administered to each test animal, thereby allowing the Agency to assess the most conservative rate that might be seen by a consumer. A study protocol submitted for Agency review before the study was conducted would have captured this incongruity. The Agency remains unwilling to agree that the proposed product is efficacious on dogs at the upper end of each weight range. Furthermore, the Agency disagrees that there is no indication that the study results obtained would be impacted by a change in the protocol to a dose titration method. The fact that there are four proposed weight-dependent doses suggests that a correlation of weight to efficacy does exist. In any case, such a conclusion cannot be made until the lowest labeled rates are tested. Figure 1 below, which appears in the Agency's 7/27/2016 review, describes the weight at which efficacy was demonstrated vs the weight at which efficacy needs to be demonstrated according to the proposed label.

FIGURE 1: WEIGHT AT WHICH EFFICACIOUS DOSE DEMONSTRATED



In regards to the materials submitted in Appendix 4, 6, and 7, new data may not be submitted as part of a rebuttal, and will not be reviewed.

Conclusion: UNACCEPTABLE. This rebuttal does not support any additional claims beyond what was already supported in the previous review (DP# 431031).

IV. EXECUTIVE DATA SUMMARY:

(A) The rebuttal does not support any additional pests or claims not already supported in the previous review (DP#

431031).

V. LABEL RECOMMENDATIONS:

(1) No changes in the Directions for Use are suggested:

(2) The following marketing claims are acceptable:

- T2.200 contains imidacloprid, permethrin, and the insect growth regulator pyriproxyfen

(3) The following marketing claims are unacceptable:

- All flea, tick, mosquito, biting fly, and lice efficacy claims are unacceptable. This includes waterproof/shampoo-proof/rainproof/water immersion claims and all IGR claims or claims against various life stages of the aforementioned pests.

(4) The following MRIDs should be removed from the data matrix, as they are classified as "unacceptable" to support the product:

49788701
49788702
49788703
49788704
49788705
49788706
49788707
49788708
49788709
49788710
49788711
49788712

(5) Note to reviewer/PM:

N/A

Fertich, Elizabeth

From: Fertich, Elizabeth
Sent: Thursday, September 01, 2016 1:49 PM
To: 'Richard L. Conn'
Cc: 'John Tatum'; IVB1; Bacon, Laura
Subject: RE: Efficacy and companion animal toxicity testing reviews for 91384-G [WARNING: SPF validation failed]
Attachments: RDEFFICACY 91384-G 20160830.pdf

Richard,
Your rebuttal was discussed on the PERC meeting on 8/30. Please see the attached memo drafted in response to the rebuttal. Let me know how you wish to proceed with this application. If you decide to cite the Bayer date, I will need a revised data matrix and the offer to pay letter.
Kind regards,
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Fertich, Elizabeth
Sent: Tuesday, August 23, 2016 3:05 PM
To: 'Richard L. Conn' <richard@connsmith.com>
Cc: John Tatum <John.Tatum@CAPSupplyInc.com>
Subject: RE: Efficacy and companion animal toxicity testing reviews for 91384-G [WARNING: SPF validation failed]

Richard,
Thanks for speaking with me today and clarifying my questions on the formulation and PRIA category. As I said, your rebuttal will be discussed at PERC on 8/30 and I will contact you after the meeting.
Kind regards,
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Richard L. Conn [mailto:richard@connsmith.com]
Sent: Tuesday, August 23, 2016 1:39 PM
To: Fertich, Elizabeth <fertich.elizabeth@epa.gov>
Cc: John Tatum <John.Tatum@CAPSupplyInc.com>
Subject: Re: Efficacy and companion animal toxicity testing reviews for 91384-G [WARNING: SPF validation failed]

Beth,
Do you think there is a reasonably good chance this item will be on the PERC agenda for their meeting August 30, a week from today?
Best regards,
Richard

On 8/22/2016 12:40 PM, Fertich, Elizabeth wrote:

> John,
> Thanks for providing the response to the efficacy and companion animal safety reviews. I have sent it to the science reviewers. The next step will be discussion at the PERC meeting. I will let you know when it is on the agenda and the results of the discussion. Based on the PERC meeting, we'll determine if a meeting is needed.
> Thanks,
> Beth
>
> Elizabeth Fertich
> US Environmental Protection Agency
> Office of Pesticide Programs
> Registration Division (7505P)
> Invertebrate and Vertebrate Branch 1 (IVB1)
> fertich.elizabeth@epa.gov
> 703-347-8560
>
> **From:** John Tatum [mailto:John.Tatum@CAPSupplyInc.com]
> **Sent:** Thursday, August 18, 2016 4:56 PM
> **To:** Fertich, Elizabeth <fertich.elizabeth@epa.gov>
> **Cc:** IVB1 <IVB1@epa.gov>; 'Richard L. Conn' <richard@connsmith.com>; 'CAP Innovet' <John.Tatum@CAPInnoVet.com>
> **Subject:** RE: Efficacy and companion animal toxicity testing reviews for 91384-G [WARNING: SPF validation failed]
>
> August 18, 2016
>
> Elizabeth Fertich
> US Environmental Protection Agency
> Office of Pesticide Programs
> Registration Division (7505P)
> Invertebrate and Vertebrate Branch 1 (IVB1)
> fertich.elizabeth@epa.gov
> 703-347-8560
>
> Subject: EPA File Symbol 91384-G
> T2.200 for Dogs
> Cover Letter to Response and Comment to Product Performance DER and Companion Animal Safety Study reviews dated July 27, 2016
>
> Dear Elizabeth:
>
> I am writing in response to EPA's Data Evaluation Record (DER) for the above-referenced studies. The DER incorrectly suggests that the submitted efficacy data from the dose confirmation studies are not acceptable because the studies were conducted using dosing at the proposed weight ranges on the label, not a titrated dose based upon animal weight. This new approach is inconsistent with EPA's

historic practice in reviewing dose confirmation data for spot on pet products, including K9 Advantix II, on which this product's substantially similar filing is based. This new approach is also inconsistent with the guidance EPA provided us at our pre-registration meeting on December 4, 2014. The methods used in the dose confirmation studies and the related efficacy data submitted to support this application are equivalent to the data on which EPA based its registration of numerous other products. The proposed rejection of claims for T2.200 therefore is inappropriate.

As explained below, we respectfully request that EPA reconsider the recommendation made in this DER and that it proceed to register this product within the current PRIA timeframe. We would like to meet with you to discuss the studies, application and timeline at your earliest convenience.

The DER is based upon a new and inappropriate approach

T2.200 for Dogs (T2) is a substantially similar formulation to K9 Advantix II Small Dog, K9 Advantix II Medium Dog, K9 Advantix II Large Dog, and K9 Advantix II Extra Large Dog, EPA Reg. Nos. 11556-141, 11556-142, 11556-143, 11556-144, respectively. The efficacy data provided from our dose confirmation studies were performed using the same approach as the studies used to register those products, and indeed many other spot on pet products. The studies were conducted in accordance with OPPTS Guideline 810.3300.

The DER package recommends against approval, reasoning that:

> While some but not all of the data submitted to support efficacy claims for this product could be adequate, the doses used throughout are not. Studies investigating the efficacy of spot-on products should determine the appropriate dose of test material based on a dose titration approach, such that all animals receive the lowest possible dose according to the proposed weight ranges. . . . It is not sufficient to apply one of the four proposed doses for each animal based on which of the four corresponding weight ranges it falls into, as was seen here. Doing so prevents study investigators and Agency reviewers from being able to determine if the product is efficacious on dogs at the very upper end of each weight range (see Figure 1 above). It is essential that the lowest labeled rate/dose is used in studies which are submitted or cited to support efficacy claims.

July 27, 2016 DER Memorandum to Elizabeth Fertich from Tim Ciarlo at page 27.

The assertion that dose confirmation studies for spot on products must use a "dose titration" approach is an abrupt, dramatic departure from EPA's practice in registering most, if not all, spot on products it bas addressed to date. CAP IM Supply relied upon that precedent and existing guidelines in investing the time and effort to design and implement the studies reviewed here. In addition, during pre-registration meetings, CAP IM Supply informed EPA about the approach it would take, and EPA did not disagree. The studies CAP IM Supply sponsored were performed by ClinVet International, which has performed many studies using this methodology that EPA has relied upon in registering spot on products. Most importantly, these studies were conducted in the same way as the studies EPA relied upon to register K9 Advantix II, the product T2.200 was expressly designed to be substantially similar to.

EPA Should Disregard the DER Insofar as they call for Dose Titration Studies

It would be dramatically unfair to CAP IM Supply for EPA to apply the expectations of this DER to its pending registration. Many existing products, including K9 Advantix II, were registered using studies designed in this way. The use of dose confirmation studies were discussed with EPA and accepted at the pre-registration meeting. EPA would be implementing a

dramatic change in the way it requires efficacy studies to be conducted without providing any notice to the regulated community, applicants or testing labs, or modifying its test guidelines. Moreover, it is clear that CAP IM Supply's studies show that its product's efficacy is substantially similar to K9 Advantix II.

For these reasons, CAP IM Supply respectfully requests that EPA disregard the conclusions in the July 27 memorandum. Instead, based upon the findings that the studies were properly conducted in accordance with the protocols used, and that the studies demonstrated the tested product's efficacy, EPA should grant CAP IM Supply's substantially similar application. If EPA determines all efficacy data for spot on products should be conducted using the dose titration method, it can and should issue a data call in for such data. Unless and until that takes place, EPA is obligated to continue to accept data generated in accordance with the longstanding EPA and registrant practice.

We have attached a technical memorandum responding to the DER in greater detail, including addressing the critique raised on specific dose confirmation and safety studies. This is a critically important issue. CAP IM Supply has been relying upon EPA completing its review of the pending application during the current PRIA time frame. Any delay will have serious business consequenses. To address the study issues as promptly as possible, we would like to meet with you in the immediate future to review EPA's position as to these studies.

The technical review can be downloaded at: [redacted]

We look forward to your response.

Sincerely,

John Tatum

COO – CAP IM Supply, Inc.

John.Tatum@CAPSupplyInc.com
801-512-7543

From: Fertich, Elizabeth [mailto:fertich.elizabeth@epa.gov]
Sent: Thursday, August 4, 2016 12:09 PM
To: Richard L. Conn <richard@connsmith.com>; John Tatum <John.Tatum@CAPSupplyInc.com>
Cc: IVB1 <IVB1@epa.gov>
Subject: Efficacy and companion animal toxicity testing reviews for 91384-G

Richard,
Please see the attached efficacy and companion animal safety reviews. There are significant deficiencies in the efficacy review and an issue with animal weights in the toxicity review. Please review the documents and contact me with any questions.
Thanks,
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs

Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

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Richard L. Conn, President, Conn & Smith, Inc.
6713 Catskill Rd, Lorton VA 22079-1113, USA
Phone: (703) 339-4199
http://www.connsmith.com

Fertich, Elizabeth

From: CAP Innovet <John.Tatum@CAPInnoVet.com>
Sent: Monday, August 22, 2016 3:29 PM
To: Fertich, Elizabeth; 'John Tatum'
Cc: IVB1; 'Richard L. Conn'; Davis, Kable
Subject: RE: Efficacy and companion animal toxicity testing reviews for 91384-G [WARNING: SPF validation failed]

Follow Up Flag: Follow up
Flag Status: Flagged

Elizabeth,

Thank you for moving this forward. We look forward to resolving as expeditiously as possible.
Please let me know if you need any other information from our team.

Best wishes,
John

John.Tatum@CAPInnoVet.com
801-512-7543

From: Fertich, Elizabeth [mailto:fertich.elizabeth@epa.gov]
Sent: Monday, August 22, 2016 12:41 PM
To: John Tatum <John.Tatum@CAPSupplyInc.com>
Cc: IVB1 <IVB1@epa.gov>; 'Richard L. Conn' <richard@connsmith.com>; 'CAP Innovet' <John.Tatum@CAPInnoVet.com>; Davis, Kable <Davis.Kable@epa.gov>
Subject: RE: Efficacy and companion animal toxicity testing reviews for 91384-G [WARNING: SPF validation failed]

John,
Thanks for providing the response to the efficacy and companion animal safety reviews. I have sent it to the science reviewers. The next step will be discussion at the PERC meeting. I will let you know when it is on the agenda and the results of the discussion. Based on the PERC meeting, we'll determine if a meeting is needed.
Thanks,
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: John Tatum [mailto:John.Tatum@CAPSupplyInc.com]
Sent: Thursday, August 18, 2016 4:56 PM
To: Fertich, Elizabeth <fertich.elizabeth@epa.gov>
Cc: IVB1 <IVB1@epa.gov>; 'Richard L. Conn' <richard@connsmith.com>; 'CAP Innovet' <John.Tatum@CAPInnoVet.com>
Subject: RE: Efficacy and companion animal toxicity testing reviews for 91384-G [WARNING: SPF validation failed]

August 18, 2016

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

Subject: EPA File Symbol 91384-G
T2.200 for Dogs
Cover Letter to Response and Comment to Product Performance DER and Companion Animal Safety Study reviews dated July 27, 2016

Dear Elizabeth:

I am writing in response to EPA's Data Evaluation Record (DER) for the above-referenced studies. The DER incorrectly suggests that the submitted efficacy data from the dose confirmation studies are not acceptable because the studies were conducted using dosing at the proposed weight ranges on the label, not a titrated dose based upon animal weight. This new approach is inconsistent with EPA's historic practice in reviewing dose confirmation data for spot on pet products, including K9 Advantix II, on which this product's substantially similar filing is based. This new approach is also inconsistent with the guidance EPA provided us at our pre-registration meeting on December 4, 2014. The methods used in the dose confirmation studies and the related efficacy data submitted to support this application are equivalent to the data on which EPA based its registration of numerous other products. The proposed rejection of claims for T2.200 therefore is inappropriate.

As explained below, we respectfully request that EPA reconsider the recommendation made in this DER and that it proceed to register this product within the current PRIA timeframe. We would like to meet with you to discuss the studies, application and timeline at your earliest convenience.

The DER is based upon a new and inappropriate approach

T2.200 for Dogs (T2) is a substantially similar formulation to K9 Advantix II Small Dog, K9 Advantix II Medium Dog, K9 Advantix II Large Dog, and K9 Advantix II Extra Large Dog, EPA Reg. Nos. 11556-141, 11556-142, 11556-143, 11556-144, respectively. The efficacy data provided from our dose confirmation studies were performed using the same approach as the studies used to register those products, and indeed many other spot on pet products. The studies were conducted in accordance with OPPTS Guideline 810.3300.

The DER package recommends against approval, reasoning that:

> While some but not all of the data submitted to support efficacy claims for this product could be adequate, the doses used throughout are not. Studies investigating the efficacy of spot-on products should determine the appropriate dose of test material based on a dose titration approach, such that all animals receive the lowest possible dose according to the proposed weight ranges. . . . It is not sufficient to apply one of the four proposed doses for each animal based on which of the four corresponding weight ranges it falls into, as was seen here. Doing so prevents study investigators and Agency reviewers from being able to determine if the product is efficacious on dogs at the very upper end of each weight range (see Figure 1 above). It is essential that the lowest labeled rate/dose is used in studies which are submitted or cited to support efficacy claims.

July 27, 2016 DER Memorandum to Elizabeth Fertich from Tim Ciarlo at page 27.

The assertion that dose confirmation studies for spot on products must use a "dose titration" approach is an abrupt, dramatic departure from EPA's practice in registering most, if not all, spot on products it has addressed to date. CAP IM Supply relied upon that precedent and existing guidelines in investing the time and effort to design and implement the studies reviewed here. In addition, during pre-registration meetings, CAP IM Supply informed EPA about the approach it would take, and EPA did not disagree. The studies CAP IM Supply sponsored were performed by ClinVet International, which has performed many studies using this methodology that EPA has relied upon in registering spot on products. Most importantly, these studies were conducted in the same way as the studies EPA relied upon to register K9 Advantix II, the product T2.200 was expressly designed to be substantially similar to.

EPA Should Disregard the DER Insofar as they call for Dose Titration Studies

It would be dramatically unfair to CAP IM Supply for EPA to apply the expectations of this DER to its pending registration. Many existing products, including K9 Advantix II, were registered using studies designed in this way. The use of dose confirmation studies were discussed with EPA and accepted at the pre-registration meeting. EPA would be implementing a dramatic change in the way it requires efficacy studies to be conducted without providing any notice to the regulated community, applicants or testing labs, or modifying its test guidelines. Moreover, it is clear that CAP IM Supply's studies show that its product's efficacy is substantially similar to K9 Advantix II.

For these reasons, CAP IM Supply respectfully requests that EPA disregard the conclusions in the July 27 memorandum. Instead, based upon the findings that the studies were properly conducted in accordance with the protocols used, and that the studies demonstrated the tested product's efficacy, EPA should grant CAP IM Supply's substantially similar application. If EPA determines all efficacy data for spot on products should be conducted using the dose titration method, it can and should issue a data call in for such data. Unless and until that takes place, EPA is obligated to continue to accept data generated in accordance with the longstanding EPA and registrant practice.

We have attached a technical memorandum responding to the DER in greater detail, including addressing the critique raised on specific dose confirmation and safety studies. This is a critically important issue. CAP IM Supply has been relying upon EPA completing its review of the pending application during the current PRIA time frame. Any delay will have serious business consequenses. To address the study issues as promptly as possible, we would like to meet with you in the immediate future to review EPA's position as to these studies.

The technical review can be downloaded at: [redacted]

We look forward to your response.

Sincerely,

John Tatum

COO – CAP IM Supply, Inc.

John.Tatum@CAPSupplyInc.com
801-512-7543

From: Fertich, Elizabeth [mailto:fertich.elizabeth@epa.gov]
Sent: Thursday, August 4, 2016 12:09 PM

To: Richard L. Conn <richard@connsmith.com>; John Tatum <John.Tatum@CAPSupplyInc.com>
Cc: IVB1 <IVB1@epa.gov>
Subject: Efficacy and companion animal toxicity testing reviews for 91384-G

Richard,
Please see the attached efficacy and companion animal safety reviews. There are significant deficiencies in the efficacy review and an issue with animal weights in the toxicity review. Please review the documents and contact me with any questions.
Thanks,
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

CAP IM Supply, Inc.
303 Perimeter Center North, Suite 300
Atlanta, GA 30346

August 17, 2016

Document Processing Desk (REGFEE)
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard Room S-4900
2777 S. Crystal Drive
Arlington, VA 22202

Attention: Elizabeth Fertich, Invertebrate and Vertebrate Branch 1 (IVB1), RD

Subject: EPA File Symbol 91384-G
T2.200 for Dogs
Response and comment to Product Performance DER and Companion Animal Safety Study reviews dated July 27, 2016

Dear Elizabeth,

PLEASE NOTE: This document contains information considered by CAP IM Supply, Inc. to be protected from disclosure as Confidential Business Information as defined by Section 10 of FIFRA.

Pages 65-73 - *Claimed confidential by submitter*

Fertich, Elizabeth

From: Fertich, Elizabeth
Sent: Monday, August 29, 2016 11:48 AM
To: Backus, Byron
Subject: RE: 91384-G DP431030

Thanks.

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Backus, Byron
Sent: Thursday, August 25, 2016 4:53 PM
To: Fertich, Elizabeth <fertich.elizabeth@epa.gov>
Subject: RE: 91384-G DP431030

First time I've ever seen an inhalation waiver presented in this way (in a data matrix), and so I probably missed it. However, as far as I'm concerned it's fine and all tox requirements have been satisfied.

Byron

From: Fertich, Elizabeth
Sent: Thursday, August 25, 2016 4:46 PM
To: Backus, Byron <Backus.Byron@epa.gov>
Subject: RE: 91384-G DP431030

Hi Byron,
I got the signed copy of the review today, thanks. The registrant pointed me to the data matrix (see attached) and said the following regarding the inhalation study...Is this acceptable?
Thanks,
Beth

In the data matrix (EPA Form 8570-35) we submitted for this product, we indicated in the "Note" column for the 870.1300 (Acute inhalation toxicity) requirement the following:

"Waiver requested due to product being liquid with low volatility and maximum 4 mL as a single dose to skin of dogs"

My prior experience has been that providing the waiver rationale in that manner (in the data matrix) was sufficient for accomplishing a waiver request for acute inhalation studies. However, if you need us to present that information in another format, we will be glad to quickly do so to address the inhalation requirement.

Elizabeth Fertich
US Environmental Protection Agency

Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Backus, Byron
Sent: Wednesday, August 24, 2016 2:19 PM
To: Mascall, Linda <Mascall.Linda@epa.gov>
Cc: Fertich, Elizabeth <fertich.elizabeth@epa.gov>; McAndrew, Eugenia <McAndrew.Eugenia@epa.gov>
Subject: 91384-G DP431030

All acute toxicity data requirements except for inhalation have been satisfied. The registrant has to address the issue of inhalation toxicity, either by conducting (or citing) an inhalation study or by making a waiver request.

Fertich, Elizabeth

From: Fertich, Elizabeth
Sent: Monday, August 29, 2016 11:49 AM
To: 'Richard L. Conn'
Cc: 'CAP Innovet'; IVB1
Subject: RE: Pending application for 91384-G: missing tox. data for 91384-G`

Richard,
The data matrix is acceptable. No further information is required for the acute inhalation data requirement.
Thanks,
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Fertich, Elizabeth
Sent: Thursday, August 25, 2016 4:46 PM
To: 'Richard L. Conn' <richard@connsmith.com>
Cc: 'CAP Innovet' <John.Tatum@CAPInnoVet.com>; IVB1 <IVB1@epa.gov>
Subject: RE: Pending application for 91384-G: missing tox. data for 91384-G`

Richard,
Thanks for providing the information for the inhalation waiver. I'm checking on the acceptability of reporting it in this manner and will get back to you soon.
Thanks,
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Richard L. Conn [mailto:richard@connsmith.com]
Sent: Wednesday, August 24, 2016 3:19 PM
To: Fertich, Elizabeth <fertich.elizabeth@epa.gov>
Cc: 'CAP Innovet' <John.Tatum@CAPInnoVet.com>; IVB1 <IVB1@epa.gov>
Subject: Re: Pending application for 91384-G: missing tox. data for 91384-G`

Beth,
In the data matrix (EPA Form 8570-35) we submitted for this product, we indicated in the "Note" column for the 870.1300 (Acute inhalation toxicity) requirement the following:

"Waiver requested due to product being liquid with low volatility and maximum 4 mL as a single dose to skin of dogs"

My prior experience has been that providing the waiver rationale in that manner (in the data matrix) was sufficient for accomplishing a waiver request for acute inhalation studies. However, if you need us to present that information in another format, we will be glad to quickly do so to address the inhalation requirement.

The most relevant data matrix is the one dated December 23, 2015 (in view of our not using the new CRP data that was presented in the June 10, 2016 data matrix).

Best regards,
Richard

On 8/24/2016 2:31 PM, Fertich, Elizabeth wrote:

> Richard,
> I got a draft review for the acute toxicity data. The reviewer provided the following comment:
>
> > All acute toxicity data requirements except for inhalation have been satisfied. The registrant has to address the issue of inhalation toxicity, either by conducting (or citing) an inhalation study or by making a waiver request.
> >
> > I will send you a copy of the final review when I receive it. In the meantime, please address the deficiency.
> >
> > Thanks,
> > Beth
>
> Elizabeth Fertich
> US Environmental Protection Agency
> Office of Pesticide Programs
> Registration Division (7505P)
> Invertebrate and Vertebrate Branch 1 (IVB1)
> fertich.elizabeth@epa.gov
> 703-347-8560

--
Richard L. Conn, President, Conn & Smith, Inc.
6713 Catskill Rd, Lorton VA 22079-1113, USA
Phone: (703) 339-4199
http://www.connsmith.com

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

August 24, 2016

MEMORANDUM:

Subject:	Name of Pesticide Product:	T2.200 FOR DOGS
	EPA Reg. No. /File Symbol:	91384-G
	DP Barcode:	DP 431030
	Decision No.:	511951
	Action Code:	R315
	Submission:	#978275
	E-Sub.	-
	PC Codes:	109701 (Permethrin: 44%) 129099 (Imidacloprid: 8.8%) 129032 (Pyriproxyfen: 0.44%)

From: Byron T. Backus, Ph.D., Toxicologist
CITAB
Registration Division (7505P)

Byron T. Backus
Aug-24-2016

Through: Masih Hashim, Ph.D., Team Leader, Toxicology
CITAB
Registration Division (7505P)

M Hashim

To: Elizabeth Fertich/Jennifer Urbanski RM 04
IVB1
Registration Division (7505P)

Registrant: CAP IM SUPPLY, INC.

FORMULATION FROM LABEL:

Active Ingredient(s):	by wt.
129099 Imidacloprid	8.80%
109701 Permethrin	44.00%
129032 Pyriproxyfen	0.44%
Other Ingredients:	46.76%
TOTAL	100.00%

ACTION REQUESTED: "Review the submitted acute toxicity data and prepare a memo. The following items are attached: 1. Cover letter; 2. Label; 3. Hard copies of studies; 4. Data matrix..."

BACKGROUND:

The material available to CITAB includes a cover letter, 6 acute toxicity studies (an acute oral LD_{50} study in MRID 49788715; a dermal LD_{50} study in MRID 49788716; two eye irritation studies in MRIDs 49788717 and 49788718; a dermal irritation study in MRID 49788719; and a Local Lymph Node Assay (LLNA) study in MRID 49788720), a data matrix (dated 12-23-15), and a label (proposed signal word: WARNING).

COMMENTS AND RECOMMENDATIONS:

1. The 6 submitted studies (oral LD_{50}; dermal LD_{50}; eye irritation [2 studies]; dermal irritation; and dermal sensitization) have been reviewed and classified as acceptable.

2. Based on the results from the acute toxicity studies, the following is a partial acute toxicity profile for 91384-G:

Oral LD_{50} (rat)	Tox. Category III	MRID 49788715	Acceptable
Dermal LD_{50} (rat)	Tox. Category IV	MRID 49788716	Acceptable
Eye Irritation (rabbit)	Tox. Category II	MRID 49788717	Acceptable
Eye Irritation (rabbit)	Tox. Category II	MRID 49788718	Acceptable
Dermal Irritation (rabbit)	Tox. Category IV	MRID 49788719	Acceptable
Sensitization (LLNA, mouse)	Positive	MRID 49788720	Acceptable

3. Based on the partial acute toxicity profile given above (and assuming assignment to toxicity category IV by inhalation exposure), the following is the precautionary and first aid labeling for 91384-G, as obtained from the Label Review System:

PRODUCT ID #: **091384-00003**

PRODUCT NAME: **T2.200 FOR DOGS**

PRECAUTIONARY STATEMENTS

SIGNAL WORD: **WARNING**

Hazards to Humans and Domestic Animals:

[Child Resistant Packaging Required].

Causes substantial but temporary eye injury. Harmful if swallowed. Do not get in eyes or on clothing. Wear protective eyewear (goggles, face shield, or safety glasses). Wash thoroughly with soap and water

after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Remove and wash contaminated clothing before reuse.

Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals.

First Aid:

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

If swallowed:
-Call a poison control center or doctor immediately for treatment advice.
-Have person sip a glass of water if able to swallow.
-Do not induce vomiting unless told to by a poison control center or doctor.
-Do not give anything to an unconscious person.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

4. All acute toxicity data requirements except for inhalation have been satisfied. The registrant has to address the issue of inhalation toxicity, either by conducting (or citing) an inhalation study or by making a waiver request.

Reviewer: Byron T. Backus, Ph.D.
Date: August 24, 2016
Risk Manager (EPA): 04

The following is the Acute Toxicity Data Evaluation Record (DER) for the acute toxicity studies (MRIDs 49788715 through 49788720) submitted in support of EPA File Symbol 91384-G:

1. DP BARCODE: 431030				
2. PC CODES: 109701 (Permethrin: 44%); 129099 (Imidacloprid: 8.8%); 129032 (Pyriproxyfen: 0.44%)				
3. CURRENT DATE: August 24, 2016				
4. TEST MATERIAL: T2; according to the registrant's cover letter dated December 3, 2015 (MRID 49788700) this is the same formulation as T2.200 for Dogs. The composition of the test item is given (p. 15 of MRID 49788715) as 44.97% Permethrin; 8.71% Imidacloprid; 0.43% Pyriproxyfen. The specific gravity was 1.144.				
Study/Species/Lab Study # /Date	**MRID**	**Results**	**Tox Cat**	**Core Grade**
Acute oral toxicity / rat / VIVOTECNIA Research S.L., Madrid, Spain / Laboratory Project ID B-01983 / October 7, 2015 / OCSPP 870.1100; OECD 425	49788715	Three fasted (overnight) female Sprague-Dawley albino rats were used. A dose of 2000 mg/kg was administered by oral gavage to three rats. All three survived. One rat had piloerection at one hour. All had "abdominal defense" (a reaction indicating that the animal has experienced pain) on the day of administration. All 3 rats had gained weight at 7 days after administration and 7 days after that. There were no gross abnormalities at necropsy. $LD_{50} > 2000$ mg/kg.	III	A
Acute dermal toxicity / rat / VIVOTECNIA Research S.L., Madrid, Spain / Laboratory Project ID B-01984 / October 9, 2015 / OCSPP 870.1200; OECD 402	49788716	There were 2 groups each with 6M & 6F Sprague-Dawley rats. Group A was treated with water; Group B was treated with 5000 mg/kg T2, with 24-hr semi-occluded exposure. There was no mortality and there were no indications of toxicity. One Group B female had barely perceptible (grade 1) erythema through Day 4. All Group B rats had weight gains between Days 0 and 7 and again between Days 7 and 14. There were no dose-related findings at necropsy. Dermal $LD_{50} > 5000$ mg/kg.	IV	A

Primary eye irritation / rabbit / VIVOTECNIA Research S.L., Madrid, Spain / Laboratory Project ID N-01986 / October 23, 2015 / OCSPP 870.2400; OECD 405	49788717	3 NZ White rabbits were used. Initial testing was with one rabbit eye, which was washed out with physiological saline at 24 hrs after instillation. Stated (p. 10 of MRID 49788717) that no corneal opacity was observed in this eye; however, sodium fluorescein test at 24 hours "revealed a mild corneal damage in the right treated eye. This damage improved on a weekly basis but had still not completely disappeared on the day of sacrifice." Photographs (p. 35-36) show little or negligible fluorescein staining on day 21. This eye was also positive for conjunctivitis (score of 2) and chemosis (score of 3) at 24 hrs, but a day later both scores were 1 (not considered positive). Two remaining eyes were washed out at 1 hour after instillation; neither of these eyes was positive for irritation effects at 24 hrs or subsequently. Assigned to toxicity category II because of positive corneal fluorescein staining of first treated eye on days 7 and 14.	II	A

Primary eye irritation / rabbit / VIVOTECNIA Research S.L., Madrid, Spain / Laboratory Project ID B-01981 / October 7, 2015 / OCSPP 870.2400; OECD 405	49788718	3 NZ White rabbits were used. Initial testing was with one rabbit eye, which was washed out with physiological saline at 1 hr after instillation. Stated (p. 11 of MRID 49788718) that no corneal opacity was observed in this eye; however, sodium fluorescein test at 24 hours "revealed a corneal damage in the right treated eye. This damage improved on a weekly basis but had still not completely disappeared on the day of sacrifice." Photographs (p. 34-35) show little or negligible fluorescein staining on day 21. This eye was also positive for conjunctivitis (score of 2) and chemosis (score of 3) at 24 hrs, but a day later both scores were 1 (not considered positive). Two remaining eyes were also washed out at 1 hour after instillation; one of these eyes was positive for grade 2 conjunctival irritation effects (redness) at 7 and 14 days. From p. 12: "Both animals showed signs of corneal damage with the fluorescein test. The corneal damage seen with the fluorescein in both animals improved on a weekly basis but had still not completely disappeared on the day of sacrifice." Photographs (p. 39-40 and 41-42) show little or negligible fluorescein staining on day 21. Assigned to toxicity category II because of positive corneal fluorescein staining in all treated eyes on days 7 and 14 and positive irritation effects in one on day 14	II	A

Primary dermal irritation / rabbit / VIVOTECNIA Research S.L., Madrid, Spain / Laboratory Project ID B-01980 / October 7, 2015 / OCSPP 870.2500; OECD 404	49788719	Two tests, an initial (1 rabbit) and confirmatory (2 rabbits) were performed. In the initial; 0.5 mL was applied at each of 3 ~6 cm^2 sites (right cranial back, left caudal back and right caudal back) on one rabbit, with exposure times of 3 min, 1 hr and 4 hrs respectively. No irritation (all scores zero) was observed in the initial test. In the confirmatory test, 2 rabbits were exposed for 4 hrs at one site (caudal back). All scores were zero at 1, 24, 48 & 72 hrs, but one rabbit had well-defined (grade 2) erythema on day 7 (possible dermal sensitization response? – note that formulation has tested positive as a dermal sensitizer in MRID 49788720).	A	IV

Local lymph node assay (LLNA)/ mouse / BSL Bioservice Munich / BSL Munich Study No. 153780 / Vivotecnia Study No. E-01982 / Ocotber 14, 2015 / OCSPP 870.2600; OECD 429	49788720	CBA/CaOlaHsd mice used, with 5 mice/group and four groups (vehicle control, 25%, 50% and 100% test material, with dilutions made in a vehicle of 1:1 v/v acetone/olive oil). Recent positive control data (1% P-Phenylaminediamine in AOO) presented. Each mouse was treated by topical application of 25 µL of the appropriate solution to the entire dorsal surface of each ear on 3 consecutive days; 5 days after first application all mice were injected in the tail vein with 250 µL of a solution containing 20 µCi ^{3}H-methyl thymidine, with sacrifice 5 hrs later. Single cell suspensions of lymph node cells from individual mice were prepared, pelleted, washed, repelleted and washed again. ^{3}H-methyl thymidine incorporation was measured using a ß-counter and expressed as disintegrations per minute (DPM), and Stimulation Indices were computed. Results: SI values: 25%: **3.6**; 50%: **4.9**; 100%: **7.8**. Test material gave positive (and concentration-dependent responses) at all dose levels tested, and must be considered (and labeled as) a dermal sensitizer.	A	Positive dermal sensi tizer

n.d. = not determined; Core Grade Key: A =Acceptable, S = Supplementary, W = Waived, U = Unacceptable, D = Data Gap

Fertich, Elizabeth

From: Richard L. Conn <richard@connsmith.com>
Sent: Thursday, July 28, 2016 2:11 PM
To: Fertich, Elizabeth
Cc: John Tatum; David Petrick; Fry, Meridith; Davis, Kable; Saunders, Jennifer
Subject: Re: EPA File Symbol 91384-G: explanatory letter from CAP IM Supply, Inc.
Attachments: Klocke stability testing T2.200 for Dogs with solvents only at 38C and 90 percent humidity.pdf

Follow Up Flag: Follow up
Flag Status: Flagged

Beth,
CAP IM Supply,Inc. wishes to proceed with the registration using the originally proposed packaging, and so we are providing here (see attached file) the Klocke lab test that John Tatum referred to in his July 22 letter as "stress testing this HPDE package in a pure solvent mixture". The pipettes in the test were filled with 3.00 mL of a 50/50 mixture of N-methylpyrrolidone and DMSO and subjected to 38 degrees C with 90 % relative humidity conditions as shown in the header rows of the 3-page Klocke lab test attached here. This was an informal stress study done for internal information purposes and was not subjected to a full QA review and approval.

CAP IM Supply has added an explanatory page to the front of the Klocke report after we noticed that some of the words in the tables within the report had not been translated to English. Most of the report shows the English translation immediately below the German words used.

We are hopeful that this information we are providing today will be sufficient to satisfy the request for the data we have mentioned earlier that showed corrosion occurring only when testing the solvents in the packaging we are proposing with this product.

Best regards,
Richard

On 7/26/2016 10:51 AM, Fertich, Elizabeth wrote:

> Richard,
> I discussed our phone conversation and your subsequent letter with the PMs and acting branch chief this morning. If you wish to proceed with the registration using the originally proposed packaging, please submit the data indicating that the corrosion occurred while testing the solvents only. We will make a determination if additional review is needed upon receipt of the data and will extend the due date as needed to accommodate the review.
>
> If you wish to use the "new" packaging proposed on 6/13, we can proceed with extending the due date to 1/28/17 and put the data into review.
>
> Thanks,
> Beth
>
> Elizabeth Fertich
> US Environmental Protection Agency
> Office of Pesticide Programs

Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Fertich, Elizabeth
Sent: Monday, July 25, 2016 10:01 AM
To: 'Richard L. Conn' <richard@connsmith.com>
Cc: John Tatum <John.Tatum@CAPSupplyInc.com>; David Petrick <David.Petrick@CAPInnoVet.com>
Subject: RE: EPA File Symbol 91384-G: explanatory letter from CAP IM Supply, Inc.

Richard,
I passed the letter on to the PMs and branch chief. We will discuss this and contact you regarding the need for a conference call.
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Richard L. Conn [mailto:richard@connsmith.com]
Sent: Friday, July 22, 2016 1:24 PM
To: Fertich, Elizabeth <fertich.elizabeth@epa.gov>
Cc: John Tatum <John.Tatum@CAPSupplyInc.com>; David Petrick <David.Petrick@CAPInnoVet.com>
Subject: EPA File Symbol 91384-G: explanatory letter from CAP IM Supply, Inc.

Hi Beth,
John Tatum today prepared the attached letter that further explains the packaging alternatives situation for T2.200 for Dogs, EPA File Symbol 91384-G. This further explanation should be helpful for the potential Tuesday (July 26) telephone discussion you and I talked about yesterday afternoon.

Best regards,
Richard

--
Richard L. Conn, President, Conn & Smith, Inc.
6713 Catskill Rd, Lorton VA 22079-1113, USA
Phone: (703) 339-4199
http://www.connsmith.com

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where is the failure in testing?

Data indicating no issue w/ current formulation in packaging

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

July 27, 2016

MEMORANDUM:

Subject:	Name of Pesticide Product:	T2.200 FOR DOGS
	EPA Reg. No. /File Symbol:	91384-G
	DP Barcode:	DP 432710
	Decision No.:	511951
	Action Code:	R315
	Submission:	#983221
	PC Codes:	109701 (Permethrin: 44.00%)
		129099 (Imidacloprid: 8.80%)
		129032 (Pyriproxyfen: 0.44%)

From: Byron T. Backus, Ph.D., Toxicologist
CITAB
Registration Division (7505P)

Byron T. Backus
July 27, 2016

Through: Masih Hashim, Ph.D., Team Leader, Toxicology
CITAB
Registration Division (7505P)

JCR for

To: Elizabeth Fertich, RM 04
IVB1
Registration Division (7505P)

Registrant: CAP IM SUPPLY, INC.

FORMULATION FROM LABEL:

Active Ingredient(s):	by wt.
129099 Imidacloprid	8.80%
109701 Permethrin	44.00%
129032 Pyriproxyfen	0.44%
Other Ingredients:	46.76%
TOTAL	100.00%

ACTION REQUESTED: "The registrant has submitted additional companion animal data in response to the 10-day letter sent on 3/8/16. The deficiency letter was sent to notify the registrant of the issues found in the review dated 2/19/16 (DP 431032). Please review the data and determine if it addresses the deficiencies identified in DP 431032... The following items are attached: 1) cover letter; 2) initial review – DP 431032; 3) hard copies of new studies."

BACKGROUND:

The material received includes a cover letter (MRID 49866900) and two MRIDs: 49866901 (Erasmus, H. (2016) A Target Animal Safety Study of T2 Applied Topically to Adult Dogs: Final Report. Project Number: CV/15/154, PN1767. Unpublished study prepared by ClinVet International (Pty) Limited. 253p.) and 49866902 (Erasmus, H. (2016) A Target Animal Safety Study of T2 Applied Topically to Puppies: Final Report. Project Number: PN1767, CV/15/155. Unpublished study prepared by ClinVet International (Pty) Limited. 152p.). MRIDs 49866901 and 49866902 are responses to a request for additional information and clarifications in a previous CITAB review (dated February 19, 2016) of two studies (MRID 49788721: Erasmus, H. (2015) A Target Animal Safety Study of T2 Applied Topically to Adult Dogs Final Report. Project Number: CV/15/154, PN1767. Unpublished study prepared by ClinVet International (Pty) Ltd. 1963p. and MRID 49788722: Erasmus, H. (2015) A Target Animal Safety Study of T2 Applied Topically to Puppies Final Report. Project Number: CV/15/155, PN1767. Unpublished study prepared by ClinVet International (Pty) Ltd. 1478p).

COMMENTS AND RECOMMENDATIONS:

1. The 44-day companion animal safety study with adult beagles (MRIDs 49788721, 49866901) has been classified as acceptable. This study supports the proposed use on adult dogs, although the proposed minimum weight (based on the results of the puppy study in MRIDs 49788722 and 49866902) should be raised to 5 lbs, and the minimum weight associated with a 2.5 mL dosage is 27 lbs. Labeling should be revised accordingly, or the registrant should provide additional information (such as the amount of dosage actually dispensed by an applicator) justifying the proposed dosages and associated weight ranges.

   The only definite adverse effects were very slight (barely perceptible) erythema observed in all test substance groups and pin point bleeding present in a single dog in group 2 following the 30-day treatment.

   Although not stated in the report or investigators' conclusions, it is noteworthy that most of the adverse effects (barely perceptible erythema in a number of dogs, mostly in Group 4, and pin point bleeding for the first 3 time points on day 30 in one group 2 [1x] dog) occurred following the second (day 30) application of the test material. The only adverse effects following the first application (day 0) were in one group 3 dog which showed very slight (barely perceptible) erythema at 3 and 4 hours following application and at the AM observation on day 1. From the information provided in the report, it is not immediately

apparent as to why these minor adverse effects were more common following the second treatment.

A group 2 male (DF5 B71) ate only 0-25% of the food offered on day 0, and a group 3 female (CBC 683) ate only 0-25% of the food offered on days 1, 2, 3 and 12 (CBC 683, along with two group 4 dogs, had been identified as "obese" in pre-clinical examinations). These were the only post application occurrences of 0-25% food consumption.

There were a number of purely cosmetic effects, including spiking ("wet paint brush effect"), white deposits on hair tips, and scaling, which cannot be considered as indicative of toxicity.

There were no indications of effects body weight or hematology and clinical chemistry parameters.

From the 870.7200 Guidelines: "The targeted adequate margin of safety is 5X. Consideration will be given to products with less than a 5X margin of safety, depending on the severity of clinical signs of toxicity (e.g. transient, non-life-threatening signs)..." The effects seen in this study (barely perceptible erythema, pinpoint bleeding in one dog after receiving a 1X application) were both transient and non-life-threatening. **On this basis, the study can be classified as acceptable in supporting the use of this product on adult (>6 months old) dogs.**

Refer to the attached DER for additional comments.

2. The 44-day companion animal safety study (MRIDs 49788721, 49866901) with beagle puppies (49-51 days old at the start of the study, weights ranging from 1.08 to 3.27 kg on day -1) has been classified as acceptable. This study supports the proposed use on puppies 7 weeks of age and older, although the proposed minimum weight should be raised to 5 lbs, and the minimum weight associated with a 2.5 mL dosage is 27 lbs. Labeling should be revised accordingly, or the registrant should provide additional information (such as the amount of dosage actually dispensed by an applicator) justifying the proposed dosages and associated weight ranges.

   No mortality occurred. All puppies survived to the end of the study.

   Individual daily observations are reported on pages 13-152 of MRID 49866902. Post-application findings are summarized on p. 30 of MRID 49788722. Findings (for both groups) included loose feces, eye discharge and diarrhea. One group 4 puppy had slight inappetance on day 1 and another had diarrhea and was listless on day 1. Both of these puppies recovered by day 2.

   From information on pages 40-42 of MRID 49788722 three group 1 puppies and nine group 4 puppies received medications for coccidia prophylaxis after day 0.

There were no indications of any effect(s) associated with exposure to the test material with respect to food consumption, body weights, or body weight gains. There were no indications of any dose-related effects involving hematology or clinical chemistry parameters.

There were cosmetic effects (spiking, greasiness, deposits on tips on hair), but no indications of pruritis and/or erythema.

The study author concluded [p. 8 of MRID 49788722] that: "The Test Substance T2, containing imidacloprid, permethrin and pyriproxyfen, administered twice within a 30-day interval at 5x the recommended dose was safe to use under the conditions of the study. An adequate margin of safety was indicated between the control group and the 5X dose as there were no toxic signs recorded in any of these groups."

This reviewer is in agreement with the stated conclusions of the study author with respect to the lack of toxicity that occurred in beagle puppies at 5x the recommended dose. In addition, the proposed minimum age of 7 weeks is supported by this study. However, the proposed label dosages and weight bands are not entirely supported by this study.

According to the proposed label dosages are 0.014 fl. oz. (0.4 mL) for 4-10 lb dogs; 0.034 fl. oz. (1.0 mL) for 11-20 lb dogs; 0.084 fl. oz. (2.5 mL) for 21-55 lb dogs; and 0.135 fl. oz. (4.0 mL) for dogs 55 lbs and over. The maximum dosages associated with these four respective weight bands would then be 0.1 mL/lb, 0.091 mL/lb; 0.119 mL/lb, and 0.073 mL/lb.

The proposed minimum weight on the label of 91384-G is 4 lbs. From information on p. 1376 the mean weight of the four lowest weight male and four lowest weight female Group 4 (5X) puppies on day -1 was 1.96 ± 0.46 kg (4.33 ± 1.01 lb), so the 5X dosage rate was 1.02 mL/kg (0.46 mL/lb). [From information on p. 1375 the mean weight of the four lowest weight male and four lowest weight female Group 1 puppies was 1.63 ± 0.38 kg (3.60 ± 0.84 lbs), so that lower weight puppies were available]. The mean 5X application rate of 1.02 mL/kg (0.46 mL/lb) supports a 1X application rate of 0.204 mL/kg or 0.0926 mL/lb. Rounding up from 4.33 lbs, it is concluded that the minimum weight supported by this study for a dosage of 0.4 mL is 5 lbs, and that the minimum weight associated with a 2.5 mL dosage is 27 lbs. The labeling should be revised accordingly, or the registrant should provide additional information (such as the amount of the product actually dispensed by an applicator) justifying the proposed dosages and associated weight ranges.

The study is classified as acceptable, provided the labeling is revised (or otherwise addressed) as indicated above.

Refer to the attached DER for additional comments.

EPA Reviewer: Byron T. Backus, Ph.D., Toxicologist
CITAB, Registration Division (7505P)

Signature: Byron T Backus
Date: July 27, 2016

EPA Secondary Reviewer: Masih Hashim, Ph.D.
CITAB, Registration Division (7505P)

Signature: _____
Date: _____

Template version 02/06

DATA EVALUATION RECORD

STUDY TYPE: Companion Animal Safety Study; adult dogs; OPPTS 870.7200

PC CODE[S]: 129099 (Imidacloprid: 8.67%); 109701 (Permethrin: 45.21%); 129032 (Pyriproxyfen: 0.42%)

DP BARCODE: 432710

TEST MATERIAL (PURITY): T2, Batch No. T2MD04; containing (from p. 19 of MRID 49788721) Imidacloprid: 8.67% w/w; Permethrin: 45.21% w/w; and Pyriproxyfen: 0.42% w/w. In an acute oral LD_{50} study (see p. 15 of MRID 49788715) with a different batch number (T2MD06, containing 44.97% Permethrin, 8.71% Imidacloprid, and 0.43% Pyriproxyfen) the test material is described as a liquid with a specific gravity of 1.144.

SYNONYM[S]: T2; T2.200 for Dogs

CITATION[S]: MRID 49788721: Erasmus, H. (2015) A Target Animal Safety Study of T2 Applied Topically to Adult Dogs Final Report. Project Number: CV/15/154, PN1767. Unpublished study prepared by ClinVet International (Pty) Ltd. 1963p.

MRID 49866901: Erasmus, H. (2016) A Target Animal Safety Study of T2 Applied Topically to Adult Dogs: Final Report. Project Number: CV/15/154, PN1767. Unpublished study prepared by ClinVet International (Pty) Limited. 253p.)

SPONSOR: (p. 11 of MRID 49788721): Omnipharm Limited, BioCity, Nottingham, UK

SUBMITTER: CAP IM SUPPLY, INC

EXECUTIVE SUMMARY: In a 44-day companion animal safety study (MRIDs 49788721, 49866901), T2 (Batch No. T2MD04), containing 8.67% w/w Imidacloprid; 45.21% w/w Permethrin; and 0.42% w/w Pyriproxyfen, was applied topically as a spot-on on Days 0 and 30 of the study. There were four groups (each consisting of 6 males and 6 females) of dogs. Group 1 (controls) received a 5X dose of mineral oil; Group 2 (1X) received a single dose of test material; Group 3 (3X) received a 3X dose of test material; and Group 4 (5X) received a 5X dose of test material. From p. 22 of MRID 49788721: "The Test/Control Substance were administered using hypodermic syringes without a needle. The correct dose volumes were drawn directly from the supplied Test/Control Substance container or were decanted into smaller

containers to prevent contamination of the supplied containers… The Test/Control Substance dose was applied topically, divided into two to four spots on the dorsal midline from the shoulders to the base of the tail… Dogs weighing up to 9.5 kg received two spots, dogs weighing >9.5 kg to 25 kg received three spots and dogs weighing more than 25 kg received four spots… The Test/Control Substance was applied directly to the skin through parting the hair until the skin was visible… Care was taken not to spill any product. No product was spilled… Dogs were restrained by hand for approximately one minute following Test/Control Substance administration, to prevent any possible run-off of the product. No run-off occurred."

From p. 21 of MRID 49788721: "Multiple doses were applied in divided doses over a period of no more than two hours." From p. 10 of MRID 49866901: "The use of multiple doses was never implemented. Due to the size of the dogs versus the Test Substance volumes applied, this was not needed. It is acknowledged that the wording in the Final Study Report does not accurately reflect this." From p. 8-10 of MRID 49788721 each Group 1 dog received 12.5 mL mineral oil on Days 0 and 30, with the exception of one female (EA0 FF6; 8.1 kg on Day -5), which received 5.0 mL mineral oil on Days 0 and 30. Each Group 2 dog received 2.5 mL test material on Days 0 and 30, each Group 3 dog received 7.5 mL test material on Days 0 and 30, and each Group 4 dog received 12.5 mL test material on Days 0 and 30.

No mortality occurred. All animals survived to the end of the study.

The study author states the following (p. 8 of MRID 49788721):

"The only Adverse Events (AEs) that could be regarded as related to the administration of the Test Substance were very slight erythema (barely perceptible) recorded in all Test Substance groups and pin point bleeding present in a single animal (5B3 E6F) in group 2. The erythema was dose related, since groups 2 and 3 had one affected animal each and group 4 had six affected animals. Group 1 [controls] had no affected animals. The pin point bleeding was an individual reaction as it occurred after administration in a single animal only. This dog also had slight erythema at the first pin point bleeding observation.

"The recommended dose for Test Substance T2, containing imidacloprid, permethrin and pyriproxyfen, administered twice within a 30 day interval at 1x, 3x and 5x, was safe to use under the conditions of the study."

From p. 11 of MRID 49866901 very slight (barely perceptible) erythema was observed in one Group 2 dog at 1 hour on Day 30, in one Group 3 dog at 3 and 4 hours on Day 0 and at the AM observation on Day 1, and in six Group 4 dogs at 1 hour on Day 30. One of the six Group 4 dogs also had very slight erythema at 2 and 3 hours on Day 30. One Group 4 dog (4E1 CA6) had erythema at two sites (midback and tailbase); the other Group 4 dogs had erythema at only one application site (either the tailbase or behind shoulder blades).

Individual daily observations are reported on p. 13-253 of MRID 49866901. The following events are listed (summarized on page 34 of MRID 49788721): Page 64: Group 1: Day 15: Dog

EA0 FF6: Vomiting; Page 99: Group 2: Day 15 (PM): Dog 5B8 FA7: Limping hind leg; Page 107: Group 2: Day 39 (AM): Dog 5BE 0DD: Vomiting; Page 164: Group 3: Day 13 (PM) to Day 15 (AM): Dog 5CD 48E: Slight limping (broken toenail); Page 243: Group 4: Day 39 (AM & PM): Dog CCF C02: Left hind foot limp.

On page 33 of MRID 49788721 it is stated that: "Other observations include pin point bleeding behind shoulder blades present in one animal (5B3 E6F) in group 2 on Day 30 for the first three time points." However, no signs ("NS") are reported for this dog on page 91 of MRID 49866901.

From p. 65 of MRID 49788721: "...pruritus (itching and scratching) was present in one animal in group 1 on Day 17. Pruritus was also present in one animal in group 3 on Day 18 at both timepoints."

Individual daily food consumption values are reported on pages 1805 to 1924 of MRID 49788721. From p. 1860 a Group 2 male (DF5 B71) consumed only 0-25% of the food offered on Day 0, and (from p. 1888) a Group 3 female (CBC 683) consumed 0-25% of the food offered on Days 1, 2, 3 and 12 (CBC 683, along with two Group 4 dogs, had been identified as "obese" in pre-clinical examinations). These were the only post application occurrences of 0-25% food consumption.

Individual body weights (taken on Days -5, -1, 9, 14, 29, 37) and body weight changes are reported on pages 1789 through 1796 of MRID 49788721. Most dogs (Group 1: 8/12; Group 2: 10/12; Group 3: 7/12; Group 4: 12/12) lost weight in tbe period from Day -1 to 9, with a maximum weight loss of 0.62 kg in a Group 3 female (CBC 683); weight losses in Group 4 dogs ranged from 0.02 to 0.40 kg (mean weight loss: 0.18 kg). It is concluded that there were no treatment-related effects on body weights or body weight changes.

There were no indications of any dose-related effects involving hematology or clinical chemistry parameters.

There were a number of purely cosmetic effects, including spiking ("wet paint brush effect"), white deposits on hair tips, and scaling, which cannot be considered as indicative of toxicity.

Although not stated in the report or investigators' conclusions, it is noteworthy that most of the adverse effects (barely perceptible erythema in a number of dogs, mostly in Group 4, and pinpoint bleeding for the first 3 time points on day 30 in one Group 2 dog) occurred following the second (day 30) application of the test material. The only adverse effects following the first application (day 0) were in one Group 3 dog (5C9 268), which showed very slight erythema (barely perceptible) at 3 and 4 hours following application and at the AM observation on day 1. From the information provided in this report, it is not immediately apparent as to why adverse effects were more common following the second treatment.

From the 870.7200 Guidelines: "The targeted adequate margin of safety is 5X. Consideration will be given to products with less than a 5X margin of safety, depending on the severity of clinical signs of toxicity (e.g. transient, non-life-threatening signs)..." The effects seen in this study (barely perceptible erythema, pinpoint bleeding in one dog after receiving a 1X application) were both transient and non-life-threatening. **On this basis, the study can be classified as acceptable in supporting the use of this product on adult (>6 months old) dogs.**

However, according to the proposed label dosages are 0.014 fl. oz. (0.4 mL) for 4-10 lb dogs; 0.034 fl. oz. (1.0 mL) for 11-20 lb dogs; 0.084 fl. oz. (2.5 mL) for 21-55 lb dogs; and 0.135 fl. oz. (4.0 mL) for dogs 55 lbs and over. The maximum dosages associated with these four respective weight bands would then be 0.1 mL/lb, 0.091 mL/lb; 0.119 mL/lb, and 0.073 mL/lb.

The proposed minimum weight on the label of 91384-G is 4 lbs. The 4 lowest weight group 4 males (13.9, 14.9, 15.7 & 16.8 kg) and the 4 lowest weight group 4 females (10.3, 10.8, 11.3 & 12.1 kg) had a mean weight of 13.23 kg, and were treated with a 5X dose of 12.5 mL test substance, or a dosage of 0.945 mL test substance/kg. This supports a maximum 1X dose of 0.189 mL/kg, or 0.086 mL/lb. Since 0.4 mL ÷ 0.086 mL/lb = 4.65 lb the minimum weight supported by this study for a dose of 0.4 mL is 5 lb (the puppy study in MRID 49788722 supports a slightly higher 1X dosage rate of 0.204 mL/kg or 0.0926 mL/lb, but because 0.4 mL ÷ 0.0926 mL/lb = 4.32 lb it would still have to be rounded up to 5 lb). The minimum weight associated with a 2.5 mL dosage (based on the puppy study in MRID 49788722) is 27 lbs.

This companion animal safety study in adult dogs (beagles) is **Acceptable** with the dosage rate revisions indicated above. It **does satisfy** the guideline requirement for a companion animal safety study (OPPTS 870.7200) in adult dogs.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and [No] Data Confidentiality statements were provided for the original study report (MRID 49468209) as well as amendment two (MRID 49724101).

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test material: T2; T2.200 for Dogs

Description:	In an acute oral LD_{50} study (see p. 15 of MRID 49788715) with a different batch number (T2MD06, containing 44.97% Permethrin, 8.71% Imidacloprid, and 0.43% Pyriproxyfen) the test material is described as a liquid with a specific gravity of 1.144.
Batch #:	Batch No. T2MD04
Purity:	Imidacloprid: 8.67% w/w; Permethrin 45.21% w/w; and Pyriproxyfen: 0.42% w/w.
Compound Stability:	Date of Manufacture (from p. 20 of MRID 49788721): 12 May 2015. The test material, in brown glass bottles, was stored at room temperature, in the dark. Stored below 25°C and protected from the sunlight.
CAS #:	52645-53-1 (Permethrin); 138261-41-3 (Imidacloprid); 95737-68-1 (Pyriproxyfen)

2. **Control:** Mineral oil

Description:	Supplied by Sigma Aldrich
Batch #:	MKBQ1755V
Purity:	Not Provided
Compound Stability:	From p. 20 of MRID 49788721: Re-test date: September 2018. To be stored at 25°C.

3. **Test animals:**

Species:	Dog	
Breed:	Beagle	
Age/weight at study initiation:	10 months to 8 years and 3 months old on Day 0. [Note: individual ages are not provided]. Males: 13.4-23.5 kg; Females: 8.1-18.2 kg [From information on p. 32-33 of MRID 49788721 one group 1 dog (963 BA4), one group 3 dog (CBC 683) and two group 4 dogs (954 CB2 and CC3 6D1) were obese].	
Source:	From the ClinVet animal colony; individually identified by subcutaneous transponders, each with unique identification.	
Housing:	Individual in cages with a floor space of ~3.0 m x 2.1 m	
Diet:	From p. 18 of MRID 49788721: "Food was supplied once a day… Animals were fed an age appropriate commercial dog diet. Dogs under the age of 12 months were fed Eukanuba puppy medium breed (Reg. no. V15464) and dogs 12 months and older were fed VetsBrands Premium adult maintenance dog food (…VetsBrands Reg. No. V24369). One dog received Purina Husky Adult…as a supplement to its normal diet for four days, as prescribed by the attending Veterinarian, to stimulate its appetite after a clinical examination revealed slight abdominal sensitivity…"	
Water:	From p. 18 of MRID 49788721 potable water was replenished at least twice a day in stainless steel bowls.	
Environmental conditions:	**Temperature:**	From p. 18 of MRID 49788721 temperature was set at ~20°C ± 4. Deviations of more than ±2°C occurred on days 10 and 11.
	Humidity:	Not reported
	Air changes:	Not reported.
	Photoperiod:	From p. 17 of MRID 49788721: 12 hours light/12 hours dark
Acclimation period:	From p. 17 of MRID 49788721: "The animals were acclimatized…for a period of 14 days before the first administration of the Test/Control Substances."	

B. STUDY DESIGN:

1. **In life dates:** From p. 23-24 of MRID 49788721: Start: 12 May 2015: start of 14-day acclimation period; 26 May 2015: first administration of test/control substance; 25 June 2015: second administration of test/control substance; 9 July 2015 (day 44 of study): end of animal phase of the study.

2. **Animal assignment:** The study design is given in Table 1. From p. 18 of MRID 49788721 the study followed a randomized block design. The 48 dogs were ranked by sex in descending order of individual body weight, and were subsequently blocked into 12 blocks of four dogs each. Animal ID numbers (in ascending order) were used to break ties. From each block of four dogs, one dog was randomly allocated to each of the four groups. Allocation of animals to groups and administration of the test or control substance was the responsibility of non-blinded personnel. All other people involved in the study were blinded to the group allocation.

TABLE 1: Study design [a]

Test Group	Total Dosing Volume/Dog (Days 0 and 30)	Mean Dose (mg/dog)[c]		Dose (mg/kg)[d]		Number assigned	
		Permethrin	Imidacloprid	Permethrin	Imidacloprid	Males	Females
1. Control	12.5 mL[b]	0	0	0	0	6	6
2. 1X	2.5 mL	1293	248	91.27	17.51	6	6
3. 3X	7.5 mL	3879	744	271.9	52.15	6	6
4. 5X	12.5 mL	6465	1240	444.5	85.26	6	6

[a] Data derived from p. 31-32 of MRID 49788721.

[b] One dog (EA0 FF6; weight 8.1 kg) in the control group received 5.0 mL of the control substance on days 0 and 30.

[c] Calculated by reviewer, using a test substance specific gravity of 1.144 g/mL, and 45.21% (w/w) Permethrin and 8.67% (w/w) Imidacloprid (the 0.42% w/w Pyriproxyfen is not included in the calculations).

[d] Based on mean Day -1 weights (p. 63 of MRID 49788721) of 14.403 kg for Group 1, 14.166 kg for Group 2, 14.267 kg for Group 3, and 14.543 kg for Group 4.

The 4 lowest weight group 4 males (13.9, 14.9, 15.7 & 16.8 kg) and the 4 lowest weight group 4 females (10.3, 10.8, 11.3 & 12.1 kg) had a mean weight of 13.23 kg, and were treated with a 5X dose of 12.5 mL test substance, or a dosage of 0.945 mL test substance/kg. This supports a maximum 1X dose of 0.189 mL/kg, or 0.086 mL/lb. The puppy study in MRID 49788722 supports a slightly higher 1X dosage rate of 0.204 mL/kg or 0.0926 mL/lb.

3. **Dose selection rationale:** The doses in this study were consistent with the 1X dosages on p. 21 of MRID 49788721 (0.4 mL/dog weighing <5 kg (<11 lbs); 1.0 mL/dog weighing 5 kg to 9.5 kg (11 lbs to 21 lbs); 2.5 mL/dog weighing 9.5 kg to 25 kg (>21 lbs to 55 lbs); 4.0 mL/dog weighing >25 kg (>55 lbs). Since the dogs in Groups 2, 3 and 4 weighed from 9.9 kg to 21.9 kg they received either 2.5 mL (Group 2: 1X), 7.5 mL (Group 3: 3X) or 12.5 mL (Group 4: 5X). Tbe doses (and associated weight ranges) given on the proposed label for 91384-G are 0.014 fl. oz. (0.4 mL) for 4-10 lb dogs; 0.034 fl. oz. (1.0 mL) for 11-20 lb dogs; 0.084 fl. oz. (2.5 mL) for 21-55 lb dogs; and 0.135 fl. oz. (4.0 mL) for dogs 55 lbs and over. The maximum dosages associated witb these four respective weight bands would then be 0.1 mL/lb, 0.091 mL/lb; 0.119 mL/lb, and 0.073 mL/lb.

4. **Treatment:** From p. 22 of MRID 49788721: "The Test/Control Substance were administered using hypodermic syringes without a needle. The correct dose volumes were drawn directly from the supplied Test/Control Substance container or were decanted into smaller containers to prevent contamination of the supplied containers... The Test/Control Substance dose was

applied topically, divided into two to four spots on the dorsal midline from the shoulders to the base of the tail… Dogs weighing up to 9.5 kg received two spots, dogs weighing >9.5 kg to 25 kg received three spots and dogs weighing more than 25 kg received four spots… The Test/Control Substance was applied directly to the skin through parting the hair until the skin was visible… Care was taken not to spill any product. No product was spilled… Dogs were restrained by hand for approximately one minute following Test/Control Substance administration, to prevent any possible run-off of the product. No run-off occurred."

From p. 21 of MRID 49788721: "Multiple doses were applied in divided doses over a period of no more than two hours." From p. 10 of MRID 49866901: "The use of multiple doses was never implemented. Due to the size of the dogs versus the Test Substance volumes applied, this was not needed. It is acknowledged that the wording in the Final Study Report does not accurately reflect this." From p. 8-10 of MRID 49788721 each Group 1 dog received 12.5 mL mineral oil on Days 0 and 30, with the exception of one female (EA0 FF6; 8.1 kg on Day -5), which received 5.0 mL mineral oil on Days 0 and 30. Each Group 2 dog received 2.5 mL test material on Days 0 and 30, each Group 3 dog received 7.5 mL test material on Days 0 and 30, and each Group 4 dog received 12.5 mL test material on Days 0 and 30.

5. **Statistics:** Food consumption: from p. 58 of MRID 49788721: "Daily food consumption was listed. Per group, the number of animals consuming their food in each of the categories was calculated over the following collection period: Day -13 to Day 44 and described using frequencies and percentages.

The categories were as follows:

Food consumption score (Fc):	Fc 1	0% to 25%;
	Fc 2	> 25% to 50%;
	Fc 3	> 50% to 75%;
	Fc 4	> 75% to 100%.

Body weight: from p. 58 of MRID 49788721: "The individual body weights and changes in body weights (absolute and percentage change) from baseline (Day -1) to the rest of the assessment days were calculated for each group and summarized using descriptive statistics. The groups were compared (2 vs 1, 3 vs 1 and 4 vs 1) with respect to the change from baseline in body weight on the post-administration days by an ANOVA with a group effect.

"An analysis of variance (ANOVA) of body weights was done to determine whether the groups differed significantly at baseline."

Specific pre- and post-administration observations: from p. 58 of MRID 49788721: "The local tolerance variables edema, erythema and eschar formation, hair effects, cosmetic changes, eye irritation and skin were listed per subject and tabulated using frequencies and percentages per group and time point."

Hematology and clinical chemistry: from p. 57 of MRID 49788721: "...the emphasis of the statistical analysis was on the change from baseline values in each of the hematology and clinical chemistry parameters. The magnitude of such changes were evaluated and presented descriptively..."

Reporting included the post-administration values that fell outside the reference range for specific laboratory parameters. In addition: "...post-administration values were compared to the baseline values in a within group comparison by means of an ANOVA with an animal and observation time (baseline, post-administration) as effects. Since the aim of the analysis was to statistically evaluate the significance of changes in parameters from baseline in conjunction with relevant clinical changes, a change from baseline that was statistically not significant ($p > 0.05$), did not necessarily indicate that the difference was not clinically relevant. Similarly, a statistically significant change from baseline should not have been necessarily interpreted as a clinically relevant finding, but should rather have been considered a finding that necessitated a careful review from a clinical point of view."

This reviewer considers the above-mentioned analyses to be acceptable.

C. METHODS:

1. Observations:

a. Post-dosing and daily observations: From p. 24 of MRID 49788721: "Specific post-administration observations were performed hourly ± 15 minutes for four hours after the end of each administration period (Days 0 and 30) and twice a day on Days 1 to 29 and Days 31 to 44... The observations included, but were not limited to, changes in skin, hair, eyes, mucous membranes, nervous signs and behavior patterns, as well as vomiting and diarrhea."

b. Clinical assessments: From p. 24 of MRID 49788721: "A veterinarian conducted a clinical examination on all dogs for enrollment and inclusion purposes... [from p. 23 of MRID 49788721 this clinical examination was on day -5]. These examinations included, but were not limited to, vital signs (pulse rate, respiratory rate and rectal temperature), mucous membranes, eyes, motility, lymph nodes, abdominal palpation, thoracic auscultation and skin condition.

There is no indication (p. 23-24 of MRID 49788721) that any clinical assessments were conducted following either the first (day 0) or second (day 30) application.

c. Application site observations: After treatment, the application site was observed twice daily for changes to the skin and fur. Any erythema/eschar and edema were scored according to the Draize scale, and the presence or absence of cosmetic changes to the hair, spiking (hair coming together in narrow, sharp points) and deposits (areas of test item visible on the surface), were also recorded.

2. **Body weight:** The dogs were weighed on days -5, -1, 0, 7, 14, 29, 37 and 44.

3. **Food consumption:** The amount of food offered daily to each dog, individual food consumption, as well as amount of food remaining, were recorded for days -14 through 44.

4. **Clinical pathology:** On days -14, 1, 7, 31 and 37 blood for hematology, clinical chemistry, and coagulation evaluation was collected. From p. 25 of MRID 49788721: "Blood specimens were collected om collection tubes for clinical chemistry on Days -14. 1 and 31. Blood specimens were also collected on Days 7 and 37 because abnormalities were recorded on Days 1 and 31. There is no indication that food was removed prior to collection.

The CHECKED (X) parameters were examined.

a. Hematology:

X	Hematocrit (HCT)*	X	Leukocyte differential count* (absolute and percentages)
X	Hemoglobin (HGB)*	X	Mean corpuscular HGB (MCH)*
X	Leukocyte count (WBC)*	X	Mean corpusc. HGB conc.(MCHC)*
X	Erythrocyte count (RBC)*	X	Mean corpusc. volume (MCV)*
X	Platelet count		Reticulocyte count
	Blood clotting measurements		Morphology (if indicated)
X	(Activated Partial Thromboplastin time) (aPTT)*		Heinz body formation
	(Clotting time)		
X	\(Prothrombin time) (PT)*		

* Recommended for companion animals safety evaluation based on the 870.7200

b. Clinical chemistry:

	ELECTROLYTES		OTHER
X	Calcium*	X	Albumin*
X	Chloride*	X	Creatinine*
	Magnesium	X	Urea nitrogen (BUN)*
X	Phosphorus*		Cholesterol
X	Potassium*	X	Globulins*
X	Sodium*	X	Glucose (random)*
	ENZYMES	X	Total bilirubin*
X	Alkaline phosphatase (ALK or ALP)*	X	Direct bilirubin*
	Cholinesterase (ChE)**		Indirect bilirubin
	Creatinine phosphokinase	X	Total protein (TP)*
	Lactic acid dehydrogenase (LDH)		Triglycerides
X	Alanine aminotransferase (ALT/also SGPT)*		Serum protein electrophoresis
X	Aspartate aminotransferase (AST/also SGOT)*		Albumin/globulin ratio
	Sorbitol dehydrogenase		
	Gamma glutamyl transferase (GGT)		
	Glutamate dehydrogenase		

* Recommended for a companion animal safety evaluation based on OPPTS 870.7200.
** Only recommended if one or more active ingredients in the formulation is a known cholinesterase inhibitor.

Reference ranges are provided (in conjunction with values not within reference ranges) for clinical chemistry (pages 40-49 of MRID 49788721) and hematology (pages 50-53 of MRID 49788721).

5. **Urinalysis:** Urinalysis is not required for companion animal safety studies and was not done as part of the current study.

6. **Sacrifice and pathology:** There were no deaths or moribund sacrifices during the study. Terminal sacrifices and gross necropsies were not done and are not required under OPPTS 870.7200.

II. RESULTS

A. **ACTUAL DOSES ADMINISTERED:** The mg/kg doses of the active ingredients are given in Table 1.

B. **OBSERVATIONS:**

1. **Clinical signs:** Selected clinical signs data are given below (from Table H, p. 34 of MRID 49788721):

Group 1		
Day	**Animal ID**	**Observation**
15	EAO FF6	Vomiting
Group 2		
7	588 FA?	Vomiting
15		Limping hind leg
39	5BE ODD	Vomiting
Group 3		
13 to 15	5CD 48E	Slight limping (broken toenail)
Group 4		
39	CCF C02	Left hind foot limp

Group 1: Dogs received the control substance
Group 2: Dogs received the test substance (single dose), T2
Group 3: Dogs received the test substance (three times the dose), T2
Group 4: Dogs received the test substance (five times the dose), T2

The following occurrences of 0-25% consumption of the total food offered on a single day are reported (summarized from data on pages 1805 to 1925 of MRID 49788721):

TABLE 2. Occurrences in Which Dogs Consumed Only 0-25% of Total Food Offered		
Group	Dog Number & Sex	Days on which there was 0-25% Consumption of Total Food Offered
2	DF5 B71 (M)	0
3	288 E14 (F)	-5
3	5D4 15D (F)	-10
3	CBC 683 (F)	2, 3, 4, 12

From information on p. 1794 of MRID 49788721 CBC 683 weighed 15.60 kg on Day -1 and 14.98 kg on Day 9, a loss of 0.62 kg. This was the maximum weight loss for any dog in any group during this time period.

With the possible exceptions of DF5 B71 (Group 2) and CBC 683 (Group 3) there was no indication of a test-related effect on food consumption.

2. **Local effects at the application site:**

From p. 34, 66 and 67 of MRID 49788721 pruritus (itching and scratching) was present in one Group 1 dog on day 17, and in one Group 3 dog on Day 18 at both time points. Very slight erythema was seen in one dog (5B3 E6F) in Group 2 on Day 30 at 1 hour [this dog also had pin point bleeding behind the shoulder blades on Day 30 for the first three time points, see below]. In Group 3 one dog had very slight erythema (barely perceptible) on Day 0 at 3 and 4 hours post-administration and on Day 1 at the first observation. In Group 4, six dogs had very slight (barely perceptible) erythema on Day 30 at one hour post-administration, with one dog still showing very slight erythema at two and three hours post-administration. All observations were at the application sites.

One Group 2 (1X) dog (5B3 E6F) had pin point bleeding behind the shoulder blades on Day 30 for the first three time points. From p. 34 of MRID 49788721: "This observation was not present on any other day or in any other group."

Other effects were cosmetic and included greasiness, spiking (wet paint brush effect), deposit on tips of hair, slight scaling, and scales (>2 mm x 2 mm). These occurred in all groups (including Group 1, which was treated with mineral oil).

4. **Mortality:** There were no deaths or moribund sacrifices.

C. **BODY WEIGHT AND WEIGHT GAIN:** Body weight data are given in Tables 3 and 4. There were no indications of any treatment-related effects on body weights or body weight gain.

TABLE 3: Mean body weight data group/sex for adult beagles treated with control/test material[a]				
Parameter/ Study day or interval	Dosage			
	Group 1 (Control) Mean Body Weight (kg) ± S.D.	Group 2 (1X) Mean Body Weight (kg) ± S.D.	Group 3 (3X) Mean Body Weight (kg) ± S.D.	Group 4 (5X) Mean Body Weight (kg) ± S.D.
Males				
Day -5	17.07 ± 3.39	16.83 ± 2.83	17.28 ± 2.89	17.01 ± 2.97
Day -1	16.55 ± 3.26	16.26 ± 2.87	16.70 ± 2.80	16.66 ± 2.94
Day 9	16.40 ± 3.14	15.99 ± 2.69	16.53 ± 2.84	16.45 ± 2.86
Day 14	16.60 ± 3.19	16.18 ± 2.62	16.71 ± 2.94	16.67 ± 2.91
Day 29	16.22 ± 2.82	16.05 ± 2.67	16.43 ± 3.00	16.59 ± 2.75
Day 37	16.28 ± 2.86	16.11 ± 2.73	16.51 ± 2.88	16.61 ± 2.88
Females				
Day -5	12.45 ± 3.33	12.54 ± 2.42	11.96 ± 2.03	12.83 ± 3.00
Day -1	12.25 ± 3.45	12.08 ± 2.27	11.83 ± 2.03	12.43 ± 2.89
Day 9	12.22 ± 3.50	12.03 ± 2.17	11.73 ± 1.79	12.29 ± 2.94
Day 14	12.27 ± 3.50	12.14 ± 2.16	11.61 ± 1.68	12.42 ± 3.02
Day 29	12.14 ± 3.64	11.98 ± 2.04	11.75 ± 1.64	12.37 ± 3.17
Day 37	12.18 ± 3.44	12.30 ± 2.20	11.91 ± 1.61	12.52 ± 3.19

[a] Calculated from individual body weights on pages 1792 through 1803 of MRID 49788721. Values are Mean ± Standard Deviation, with n=6 for all groups/sex.

TABLE 4: Mean weight changes group/sex of adult beagles treated with control or test material[a]				
Parameter/ Study day or interval	Dosage			
	Group 1 (Control) Mean Body Weight Change (kg) ± S.D.	Group 2 (1X) Mean Body Weight Change (kg) ± S.D.	Group 3 (3X) Mean Body Weight Change (kg) ± S.D.	Group 4 (5X) Mean Body Weight Change (kg) ± S.D.
Males				
BW change (kg):				
Days -1 to 9	-0.155 ± 0.225	-0.265 ± 0.226	-0.173 ± 0.150	-0.207 ± 0.129
Days 9 to 14	0.200 ± 0.078	0.193 ± 0.207	0.182 ± 0.137	0.222 ± 0.110
Days 14 to 29	-0.375 ± 0.472	0.130 ± 0.228	-0.280 ± 0.178	-0.048 ± 0.225
Days 29 to 37	0.060 ± 0.194	0.057 ± 0.265	0.078 ± 0.146	0.018 ± 0.155
Days 37 to 44	0.082 ± 0.107	0.057 ± 0.239	0.092 ± 0.175	0.050 ± 0.080
Days -1 to 44	-0.188 ± 0.689	-0.088 ± 0.327	-0.102 ± 0.318	0.005 ± 0.183
Females				
BW change (kg):				
Days -1 to 9	-0.033 ± 0.111	-0.048 ± 0.158	-0.102 ± 0.266	-0.143 ± 0.097
Days 9 to 14	0.052 ± 0.053	0.108 ± 0.198	-0.123 ± 0.192	0.135 ± 0.172
Days 14 to 29	-0.137 ± 0.283	-0.162 ± 0.390	0.137 ± 0.165	-0.048 ± 0.416
Days 29 to 37	0.040 ± 0.263	0.322 ± 0.196	0.073 ± 0.178	0.148 ± 0.182
Days 37 to 44	0.122 ± 0.095	-0.098 ± 0.203	0.030 ± 0.236	0.033 ± 0.125
Days -1 to 44	0.043 ± 0.353	0.122 ± 0.565	0.102 ± 0.362	0.125 ± 0.623

[a] Calculated from individual body weights on pages 1792 through 1803 of MRID 49788721. Values are Mean ± Standard Deviatioo, with n=6 for all groups/sex.

The following is from p. 129 of MRID 49788721:

The following table displays the p-values regarding the change from baseline (Day -1) comparison between the groups.

		p-values				
Parameter	Comparison	Day 9	Day 14	Day 29	Day 37	Day 44
Weight (kg)	2 - 1	0.4122	0.7167	0.6560	0.2233	0.6319
	3 - 1	0.5688	0.1796	0.7873	0.5119	0.6967
	4 - 1	0.2901	0.7839	0.3184	0.2554	0.4609

Group 1: Dogs received the control substance
Group 2: Dogs received the test substance (single dose), T2
Group 3: Dogs received the test substance (three times the dose), T2
Group 4: Dogs received the test substance (five times the dose), T2

There is no indication of any significant difference, although the p-values above were calculated only for all dogs (males and females) in each group [they should also have calculated for separate sexes]. However, given the relatively small weight changes shown in Table 4, it is unlikely there would be any statistical significance.

D. FOOD CONSUMPTION:

The following table shows incidences of food consumption ranges on the days (0 and 30) of application of the test material as well as the two subsequent days.

TABLE 5. Incidences of Food Consumption on Days of Application and Subsequent Two Days[a]

	Amount of Offered Food Consumed			
	0-25%	25-50%	50%-75%	75-100%
Group 1				
Day 0*	0/12	0/12	0/12	12/12
Day 1	0/12	0/12	2/12	10/12
Day 2	0/12	0/12	0/12	12/12
Day 30*	0/12	0/12	1/12	11/12
Day 31	0/12	0/12	2/12	10/12
Day 32	0/12	0/12	2/12	10/12
Group 2				
Day 0*	0/12	0/12	2/12	10/12
Day 1	1/12	1/12	1/12	9/12
Day 2	0/12	0/12	1/12	11/12
Day 30*	0/12	0/12	0/12	12/12
Day 31	0/12	0/12	1/12	11/12
Day 32	0/12	0/12	1/12	11/12
Group 3				
Day 0*	0/12	1/12	0/12	11/12
Day 1	0/12	0/12	0/12	12/12
Day 2	0/12	0/12	0/12	12/12
Day 30*	0/12	0/12	0/12	12/12
Day 31	0/12	0/12	1/12	11/12
Day 32	0/12	0/12	0/12	12/12
Group 4				
Day 0*	0/12	0/12	0/12	12/12
Day 1	0/12	0/12	0/12	12/12
Day 2	0/12	0/12	0/12	12/12
Day 30*	0/12	0/12	0/12	12/12
Day 31	0/12	0/12	0/12	12/12
Day 32	0/12	0/12	0/12	12/12

[a] Data taken from pages 110 – 117 of MRID 49788721.

* Days of Application

It is noteworthy that all dogs in Group 4 consumed the maximum amount of food (75-100%) on the days of application as well as the two subsequent days.

E. BLOOD ANALYSES:

1. Hematology and coagulation parameters:

From p. 38 of MRID 49788721: "Hematology results are described in Appendix B, Section 2.1. The frequency of values that were not within the reference ranges were tabulated in Appendix A, Table N... None of the values reported out of range were of clinical relevance."

After examining Appendix A, Table N (pages 50-53 of MRID 49788721) this reviewer concludes there was nothing of any clinical significance and there was no indication of an effect involving exposure to the test material.

2. Clinical chemistry:

The following significant clinical chemistry values are reported on p. 37 of MRID 49788721:

Table J Summary of clinical chemistry abnormalities

Group	ID	Parameter (reference range u/L)	Study day	Value
3	CBC 683	ALP (26 to 146)	37	549
		ALT (21 to 60)		558
4	954 CB2	ALP (26 to 146)	-14	137
			1	212
			7	228
			31	253
			37	228
	E9E E30	ALP (26 to 146)	-14	120
			31	203
			37	177

Group 3: Dogs received the test substance (three times the dose), T2
Group 4: Dogs received the test substance (five times the dose), T2

From p. 37 of MRID 49788721:

All of these animals were clinically healthy and had no other abnormalities.

None of the other values reported out of range were of clinical relevance.

The elevated ALP and ALT in CBC 683 (Group 3) were recorded once in the study.

In Group 4 ALP only was elevated in 954 CB2 on 5 occasions and in E9E E30 on three occasions.

These values are non-specific and not indicative of a disease or serious tissue damage.

These enzymes occur in different tissues and when a single enzyme is increased it does not necessarily indicate a specific condition. In liver disease more than one liver enzyme, particularly ALP and GGT, is expected to be elevated and if the test item caused such a condition a dose relationship is expected which is not the case in this study. ALP has various isoenzymes that can be elevated in liver disease, endogenous or exogenous corticosteroid activity, bone or intestinal conditions.

ALT is usually elevated with AST in liver disease but can also be elevated in muscle necrosis, corticosteroid activity, various drugs and trauma.

The animals were clinically healthy, no dose relationship is evident, and no liver condition or other adverse condition can be diagnosed from these figures.

Refer Clinical Pathology, fourth edition, Latimer, Mahaffey and Prasse.

A. INVESTIGATORS' CONCLUSIONS:

The study author states the following (p. 8 of MRID 49788721):

"The only Adverse Events (AEs) that could be regarded as related to the administration of the Test Substance were very slight erythema (barely perceptible) recorded in all Test Substance groups and pin point bleeding present in a single animal (5B3 E6F) in group 2. The erythema was dose related, since groups 2 and 3 had one affected animal each and group 4 had six affected animals. Group 1 [controls] had no affected animals. The pin point bleeding was an individual reaction as it occurred after administration in a single animal only. This dog also had slight erythema at the first pin point bleeding observation.

"The recommended dose for Test Substance T2, containing imidacloprid, permethrin and pyriproxyfen, administered twice within a 30 day interval at 1x, 3x and 5x, was safe to use under the conditions of the study."

B. REVIEWER'S COMMENTS:

Although not stated in the report or investigators' conclusions, it is noteworthy that most of the adverse effects (barely perceptible erythema in a number of dogs, mostly in Group 4, and pinpoint bleeding for the first 3 time points on day 30 in one Group 2 dog) occurred following the second (day 30) application of the test material. The only adverse effects following the first application (day 0) were in one Group 3 dog (5C9 268), which showed very slight erythema (barely perceptible) at 3 and 4 hours following application and at the AM observation on day 1. From the information provided in this report, it is not immediately apparent as to why adverse effects were more common following the second treatment.

From the 870.7200 Guidelines: "The targeted adequate margin of safety is 5X. Consideration will be given to products with less than a 5X margin of safety, depending on the severity of clinical signs of toxicity (e.g. transient, non-life-threatening signs)..." The effects seen in this study (barely perceptible erythema, pinpoint bleeding in one dog after receiving a 1X application) were both transient and non-life-threatening. **On this basis, we can classify the study as acceptable and as supporting the use of this product on adult (>6 months old) dogs.**

However, according to the proposed label dosages are 0.014 fl. oz. (0.4 mL) for 4-10 lb dogs; 0.034 fl. oz. (1.0 mL) for 11-20 lb dogs; 0.084 fl. oz. (2.5 mL) for 21-55 lb dogs; and 0.135 fl. oz. (4.0 mL) for dogs 55 lbs and over. The maximum dosages associated with these four respective weight bands would then be 0.1 mL/lb, 0.091 mL/lb; 0.119 mL/lb, and 0.073 mL/lb.

The proposed minimum weight on the label of 91384-G is 4 lbs. The 4 lowest weight group 4 males (13.9, 14.9, 15.7 & 16.8 kg) and the 4 lowest weight group 4 females (10.3, 10.8, 11.3 & 12.1 kg) had a mean weight of 13.23 kg, and were treated with a 5X dose of 12.5 mL test substance, or a dosage of 0.945 mL test substance/kg. This supports a maximum 1X dose of 0.189 mL/kg, or 0.086 mL/lb. Since 0.4 mL ÷ 0.086 mL/lb = 4.65 lb the minimum weight supported by this study for a dose of 0.4 mL is 5 lb (the puppy study in MRID 49788722 supports a slightly higher 1X dosage rate of 0.204 mL/kg or 0.0926 mL/lb, but because 0.4 mL ÷ 0.0926 mL/lb = 4.32 lb it would still have to be rounded up to 5 lb).

C. STUDY DEFICIENCIES:

While the study did not use a concurrent vehicle control group, this is not a requirement (only a recommendation) in the current 870.7200 Companion Animal Safety Guidelines.

There is no reporting of individual ages (the only information as to ages is on page 17 of MRID 49788721 which states ages ranged from 10 months to 8 years and 3 months on Day 0). In addition, from information on pages 32-33 of MRID 49788721 one group 1 dog (963 BA4), one group 3 dog (CBC 683) and two group 4 dogs (954 CB2 and CC3 6D1) were

obese. However, reporting of the ages of individual adult animals and exclusion of obese animals are not requirements that are specified in the 870.7200 Guidelines.

The following is the Acute Toxicity Data Evaluation Record (DER) for the companion animal (adult beagle) safety study submitted for EPA File Symbol 91384-G which was conducted on T2, Batch No. T2MD04

1. DP BARCODE: 432710				
2. PC CODES (of proposed product): 129099 (Imidacloprid: 8.67%); 109701 (Permethrin: 45.21%); 129032 (Pyriproxyfen: 0.42%)				
3. CURRENT DATE: July 27, 2016				
4. TEST MATERIAL: T2, Batch No. T2MD04; containing (from p. 19 of MRID 49788721) Imidacloprid: 8.67% w/w; Permethrin: 45.21% w/w; and Pyriproxyfen: 0.42% w/w. In an acute oral LD_{50} study (see p. 15 of MRID 49788715) with a different batch no (T2MD06, containing 44.97% Permethrin, 8.71% Imidacloprid, and 0.43% Pyriproxyfen) the test material is described as a liquid with a specific gravity of 1.144.				
Study/Species/Lab Study # /Date	**MRID**	**Results**	**Tox Cat**	**Core Grade**
Companion animal safety / dog (adult beagle) / Clin Vet International, Bloemfontein, South Africa / Project No. CV/15/154, PN1767/ December 3, 2015 / OCSPP 870.7200 Companion animal safety / dog adult beagle (Report Supplement) / Clin Vet International, Bloemfontein, South Africa / Project No. CV/15/154, PN1767/ March 18, 2016/ OCSPP 870.7200	49788721 49866901	There were 4 groups, each consisting of 6M & 6F adult (10 months to 8 years and 3 months on Day 0) beagles. Day -1 weights: M: 13.4-23.5 kg; F: 8.1-18.2 kg. Dogs were topically exposed to control or test substance on Days 0 & 30. Study went to day 44. Group 1 received 5x dose of mineral oil (12.5 mL, except 1 female which received 5.0 mL); Group 2 received 1x (2.5 mL) test substance; Group 3 received 3x (7.5 mL) test substance; Group 4 received 5x (12.5 mL). No mortality; all dogs survived to end of study. There were no effects on body weight, or hematology and clinical chemistry parameters. One Group 2 male ate only 0-25% of the food offered on Day 0, and a Group 3 female ate only 0-25% of the food offered on Days 1, 2, 3 and 12. These were the only post application occurrences of 0-25% food consumption. Adverse effects, almost all following 30-day treatment, were barely perceptible erythema in a number of dogs, mostly from Group 4, and pinpoint bleeding in one Group 2 dog, considered to be both transient and non-life threatening. Maximum 1X dose supported is 0.086 mL/lb, so minimum weight supported by 0.4 mL dose is 5 lb (4.65 lb rounded up).	N/A	A (with label revision)

n.d. = not determined; Core Grade Key: A =Acceptable, S = Supplementary, W = Waived, U = Unacceptable, D = Data Gap

EPA Reviewer: Byron T. Backus, Ph.D., Toxicologist
CITAB, Registration Division (7505P)

Signature: Byron T Backus
Date: July 27, 2016

EPA Secondary Reviewer: Masih Hashim, Ph.D.
CITAB, Registration Division (7505P)

Signature: JCR for
Date: July 27, 2016

Template version 02/06

DATA EVALUATION RECORD

STUDY TYPE: Companion Animal Safety Study; puppy; OPPTS 870.7200

PC CODE[S]: 129099 (Imidacloprid: 8.67%); 109701 (Permethrin: 45.21%); 129032 (Pyriproxyfen: 0.42%)

DP BARCODE: 432710

TEST MATERIAL (PURITY): T2, Batch No. T2MD06; containing (from p. 21 of MRID 49788722) Imidacloprid: 8.71% w/w; Permethrin: 44.97% w/w; and Pyriproxyfen: 0.43% w/w. In an acute oral LD_{50} study (see p. 15 of MRID 49788715) with the same batch number (T2MD06) the test material is described as a liquid with a specific gravity of 1.144.

SYNONYM[S]: T2; T2.200 for Dogs

CITATION[S]: MRID 49788722: Erasmus, H. (2015) A Target Animal Safety Study of T2 Applied Topically to Puppies Final Report. Project Number: CV/15/155, PN1767. Unpublished study prepared by ClinVet International (Pty) Ltd. 1478p

MRID 49866902: Erasmus, H. (2016) A Target Animal Safety Study of T2 Applied Topically to Puppies: Final Report. Project Number: PN1767, CV/15/155. Unpublished study prepared by ClinVet International (Pty) Limited. 152p.

SPONSOR: (from information on pages 3 and 12 of MRID 49788722): Omnipharm Limited, BioCity, Pennyfoot Street, Nottingham, UK

SUBMITTER: CAP IM SUPPLY, INC

EXECUTIVE SUMMARY: In a 44-day companion animal safety study (MRIDs 49788721, 49866901), T2 (Batch No. T2MD04), containing 8.67% w/w Imidacloprid; 45.21% w/w Permethrin; and 0.42% w/w Pyriproxyfen, was applied topically on Days 0 and 30 as a spot-on. There were two groups (each consisting of 6 males and 6 females) of beagle puppies (49-51 days old at the start of the study, weights ranging from 1.08 to 3.27 kg on day -1).

Group 1 (controls) received a 5X dose of mineral oil and Group 4 (5X) received a 5X dose of test material. From p. 22-23 of MRID 49788722: "The Test/Control Substance was administered using hypodermic syringes without a needle. The correct dose volumes were drawn directly

from the supplied Test/Control Substance container… The Test/Control Substance dose was applied topically, divided in two to four spots on the dorsal midline from the shoulders to the base of the tail. All pups weighed less than 9.5 kg and received two spots. Multiple doses were applied in divided doses over a period of no more than two hours to the pups in groups 1 and 4."

From p. 9 of MRID 49866902: "Only one animal (57B 202 in group 4) on Day 30 received its Test Substance in two doses of 3.0 mL and 2.0 mL, 12 minutes apart at the same site of administration… The reason for this was that this was one of the smallest *[actually it weighed 4.91 kg, but it was receiving a total dose of 5.0 mL rather than the 2.0 mL that most others received]* puppies…and it was considered that applying a split dose would be appropriate in order to avoid runoff, which could have resulted in an incomplete dose being administered. The site of administration was not allowed to dry before the second administration, since based on past experience, this normally takes longer than the allowed two hours."

No mortality occurred. All puppies survived to the end of the study.

Individual daily observations are reported on pages 13-152 of MRID 49866902. Post-application findings are summarized on p. 30 of MRID 49788722. Findings (for both groups) included loose feces, eye discharge and diarrhea. One group 4 puppy had slight inappetance on day 1 and another had diarrhea and was listless on day 1. Both of these puppies recovered by day 2.

From information on pages 40-42 of MRID 49788722 three group 1 puppies and nine group 4 puppies received medications for coccidia prophylaxis after day 0.

Individual daily food consumption values are reported on pages 1382 to 1441 of MRID 49788722. There were 7 post-treatment (day 0 to day 44) occurrences of 0-25% food consumption in group 1 puppies, and 8 occurrences in group 2 puppies, with no indications of any effect(s) associated with exposure to the test material.

Puppies were weighed on days -1, 7, 14, 29, 37 and 44. There were no indications of any treatment-related effects on body weights or body weight gains.

Incidences of "local" (application site?) effects are reported on pages 115-161 of MRID 49788722. Only cosmetic effects (spiking, greasiness, deposits on tips on hair) were observed. There were no observations of pruritis and/or erythema.

There were no indications of any dose-related effects involving hematology or clinical chemistry parameters.

The study author concluded [p. 8 of MRID 49788722] that: "The Test Substance T2, containing imidacloprid, permethrin and pyriproxyfen, administered twice within a 30-day interval at 5x the recommended dose was safe to use under the conditions of the study. An adequate margin of

safety was indicated between the control group and the 5X dose as there were no toxic signs recorded in any of these groups."

This reviewer is in agreement with the stated conclusions of the study author with respect to the lack of toxicity that occurred in beagle puppies at 5x the recommended dose. In addition, the proposed minimum age of 7 weeks is supported by this study. However, the proposed label dosages and weight bands are not entirely supported by this study.

According to the proposed label dosages are 0.014 fl. oz. (0.4 mL) for 4-10 lb dogs; 0.034 fl. oz. (1.0 mL) for 11-20 lb dogs; 0.084 fl. oz. (2.5 mL) for 21-55 lb dogs; and 0.135 fl. oz. (4.0 mL) for dogs 55 lbs and over. The maximum dosages associated with these four respective weight bands would then be 0.1 mL/lb, 0.091 mL/lb; 0.119 mL/lb, and 0.073 mL/lb.

The proposed minimum weight on the label of 91384-G is 4 lbs. From information on p. 1376 the mean weight of the four lowest weight male and four lowest weight female Group 4 (5X) puppies on day -1 was 1.96 ± 0.46 kg (4.33 ± 1.01 lb), so the 5X dosage rate was 1.02 mL/kg (0.46 mL/lb). [From information on p. 1375 the mean weight of the four lowest weight male and four lowest weight female Group 1 puppies was 1.63 ± 0.38 kg (3.60 ± 0.84 lbs), so that lower weight puppies were available]. The mean 5X application rate of 1.02 mL/kg (0.46 mL/lb) supports a 1X application rate of 0.204 mL/kg or 0.0926 mL/lh. Rounding up from 4.33 lbs, it is concluded that the minimum weight supported by this study for a dosage of 0.4 mL is 5 lbs, and that the minimum weight associated with a 2.5 mL dosage is 27 lbs. The labeling should be revised accordingly, or the registrant should provide additional information (such as the amount of the product actually dispensed by an applicator) justifying the proposed dosages and associated weight ranges.

The study is classified as acceptable, provided the labeling is revised (or otherwise addressed) as indicated above.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and No Data Confidentiality Claims statements were provided for the original study report (MRID 49788722) as well as the report supplement (MRID 49866902).

I. MATERIALS AND METHODS

A. MATERIALS:

1. **Test material:**		T2; T2.200 for Dogs
	Description:	In an acute oral LD_{50} study (see p. 15 of MRID 49788715) with the same batch number (T2MD06, containing 44.97% Permethrin, 8.71% Imidacloprid, and 0.43% Pyriproxyfen) the test material is described as a liquid with a specific gravity of 1.144.
	Batch #:	Batch No. T2MD06
	Purity:	Imidacloprid: 8.71% w/w; Permethrin 44.97% w/w; and Pyriproxyfen: 0.43% w/w.
	Compound Stability:	
	CAS #:	138261-41-3 (Imidacloprid); 52645-53-1 (Permethrin); 95737-68-1 (Pyriproxyfen)

2. Vehicle control: From p. 21 of MRID 49788722; Mineral oil

Description:	No description provided
Batch #:	(From p. 21 of MRID 49788722): MKBQ1755V
Purity:	Not Provided
Compound Stability:	No indication in the report that the vehicle control was tested for stability, although the expiration date is reported (p. 21 of MRID 49788722) as September, 2018. The control substance was stored at below 25.0°C.

3. Test animals:

Species:	Dog
Breed:	Beagle
Age/weight at study initiation:	(From p. 17 of MRID 49788722): 49-51 days old; 1.08-3.27 kg on day -1.
Source:	From the ClinVet animal colony. They were identified with subcutaneous transponders with unique alpha numeric codes
Housing:	(From p. 17 of MRID 49788722): "Puppies were housed individually in suitably partititioned, individual, adult dog cages… Limited direct contact between two pups housed in the same adult dog cage was possible through the metal grid partition separating them. Only puppies in the same group were housed together in a divided adult cage…" The floor size for each puppy was 1.5 m x 2.1 m."
Diet:	(From p. 18 of MRID 49788722): "Food was supplied twice a day, with puppies receiving half of their daily ration in the morning and half in the afternoon… Animals were fed an age appropriate commercial dog diet Eukanuba puppy medium breed (Reg. no. V15464). Individual animals received Hill's puppy medium (Reg. no. V11863). Appropriate wet food (Purina Husky Puppy, Reg. no. V10430) was added by the Veterinarian for individual animals." From information on pp. 1382-1441 of MRID 49788722 the puppies were originally offered 0.5 cup of food/day, but this was increased on days 33 or 36 to 0.75 cup/day for 7 puppies in Group 1 and 7 puppies in Group 4.
Water:	(From p. 18 of MRID 497887220: "…potable water was replenished at least twice a day in stainless steel bowls."
Environmental conditions:	**Temperature:** (From p. 18 of MRID 49788722): temperature was set at 20° ± 4°C. Deviations for short periods of time occurred. (From p. 43 of MRID 49788722): "Temperatures in the cage environment ranged from 13.4°C to 27.0°C…" **Humidity:** (From p. 43 of MRID 49788722): "…relative humidity ranged from 17.4% to 59.4%." **Air changes:** Not reported. (There is a heading on p. 18 of MRID 49788722 for "Thermo-regulation and ventilation." However, there is no information as to ventilation or air changes). **Photoperiod:** 12 hours light/12 hours dark
Acclimation period:	(From p. 18 of MRID 49788722): "The animals were acclimitised…for a period of at least 14 days before the first administration of the Test/Control Substances."

B. STUDY DESIGN:

1. **In life dates:** From p. 12 of MRID 49788722: "The study was conducted in phases as 7 week-old puppies became available." The first phase had an experimental start date (Day 0 = day of first application) of June 24, 2015. The second application day (Day 30) was July 24, 2015 and the termination date (Day 44) was August 7, 2015. The last phase (Phase 5) had a start date (Day 0) of August 19, 2015, a second application on September 18, 2015 and a termination (Day 44) date of October 2, 2015.

2. **Animal assignment:** The study design is given in Table 1. From p. 19 of MRID 49788722: "The study followed a randomized block design. The study was conducted in phases as the animals reached the inclusion age. Two tables were prepared, one for female pups and one for male pups. Both tables were divided into six blocks of two pups each to accommodate the 24 pups... As soon as a pup had reached the correct age, it was entered in the first available space of the first incomplete block, according to its sex. If more than one pup of the same sex had reached the inclusion age on the same day, they were ranked in ascending order of ID and entered into the table in that order."

TABLE 1: Study design [a]

Test Group	Total Dosing volume	Mean Dose (mg/puppy)[b]		Dose (mg/kg)[c]		Number assigned	
		Permethrin	Imidacloprid	Permethrin	Imidacloprid	Males	Females
1. Control	2.0 mL/puppy < 5 kg* 5.0 mL/puppy 5-9 kg 12.5 mL/puppy 9-25 kg	0	0	0	0	6	6
4. 5X	2.0 mL/puppy < 5 kg* 5.0 mL/puppy 5-9 kg 12.5 mL/puppy 9-25 kg	1027	199			6	6

* Since the puppies weighed 1.08-3.27 kg on Day -1, they were all dosed with 5 x 0.4 mL test/control substance on Day 0.

[a] Data derived from p. 22 of MRID 49788722.

[c] Calculated by reviewer, using a test substance specific gravity of 1.144 g/mL, and 44.9% (w/w) Permethrin and 8.71% w/w Imidacloprid.

From pages 8-9 of MRID 49866902 two controls, 698 0C0 (4.9 kg on Day 29) and 698 4D1 (6.05 kg on Day 29) each received 5.0 mL control item on Day 30, while four group 4 puppies, 5A3 1B0 (5.1 kg on Day 29), 5C3 CC8 (5.54 kg on Day 29), 5D1 0EA (4.94 kg on Day 29), and 57B 202 (4.91 kg on Day 29) each received 5.0 mL of the test substance.

3. **Dose selection rationale:** The 1X dosage level for a puppy < 5 kg in this study was 0.4 mL/kg. The proposed label dosages are 0.014 fl. oz. (0.4 mL) for 4-10 lb (1.81-4.54 kg) dogs; 0.034 fl. oz. (1.0 mL) for 11-20 lb (5.0-9.07 kg) dogs; 0.084 fl. oz. (2.5 mL) for 21-55 lb (9.53-24.9 kg) dogs; and 0.135 fl. oz. (4.0 mL) for dogs 55 lbs (24.9 kg) and over. The study initially included two additional groups: a Group 2 (1X) and a Group 3 (3X). The puppies in these two groups presumably received a day 1 application of test material, but

were sham-treated with control material on day 30 (personnel conducting this study were blinded as to which dosage group individual puppies were in).

4. **Treatment:** From p. 23 of MRID 49788722: "The Test/Control Substance dose was applied topically, divided in two to four spots on the dorsal midline from the shoulders to the base of the tail. All pups weighed less than 9.5 kg and received two spots. Multiple doses were applied in divided doses over a period of no more than two hours to the pups in groups 1 and 4." From p. 9 of MRID 49866902: "Only one animal (57B 202 in group 4) reeeived its Test Substance in two doses of 3.0 mL and 2.0 mL, 12 minutes apart at the same site of administration... The reason for this was that this was one of the smallest puppies in the phase, and it was considered that applying a split dose would be appropriate in order to avoid run off, which could have resulted in an incomplete dose being administered. The site of administration was not allowed to dry before the second administration, since based on past experience this normally takes longer than the allowed two hours."

   The following comment was previously made by this reviewer in a memorandum dated February 19, 2016 for 91384-G: "...draft labelling (submitted December 3, 2015) states (p. 11) that for dogs weighing 4-10 lbs and 11-20 lbs: "Apply the entire contents of the applicator to one spot as shown." This spot would be on the dog's back between the shoulder blades, so there is an inconsistency between the way the test/control materials were applied (to 2 spots) in this study and the directions for use. This inconsistency has to be addressed." The registrant has responded with the following (p. 10 of MRID 49866902): "As this was a safety study, the doses to be applied were 5x the standard dose that will be administered in practice. This obviously results in a much larger volume of product being applied than will happen in the field. Due to the small size of the puppies, the dose was administered in two spots rather than one, in order to minimise run-off and ensure that each puppy received its entire dose."

5. **Statistics:** From p. 53 of MRID 49788722: "The local tolerance variables of edema, erythema and eschar formation, hair effects, cosmetic changes, eye irritation and skin were listed per subject and tabulated using frequencies and percentages per group and time point."

   For body weight (p. 53 of MRID 49788722): "The individual body weights and changes in body weights (absolute and percentage change) from baseline (Day -1) to the rest of the assessment days were calculated for each group, and summarized using descriptive statistics. The groups were compared (4 vs 1) with respect to the change from baseline in body weight on the post-administration days by an ANOVA with a group effect."

   For food consumption (p. 53 of MRID 49788722): "Daily food consumption was listed. Per group, the number of animals consuming their food in each of the categories was calculated over the following collection period: Day -13 to Day 44 and described using frequencies and percentages."

   The categories were as follows:

Food consumption score (Fc):	Fc 1	0% to 25%
	Fc 2	> 25% to 50%
	Fc 3	> 50% to 75%
	Fc 4	> 75% to 100%

For clinical pathology (p. 52 of MRID 49788722): "...the emphasis of the statistical analysis was on the change from baseline values in each of the hematology and clinical chemistry parameters. The magnitude of such changes were evaluated and presented descriptively. The clinical relevance and interpretation from a clinical point of view were described in the study report..."

This reviewer considers these analyses to be acceptable.

C. METHODS:

1. Observations:

a. General health observations: From p. 25 of MRID 49788722 (daily observations): "These observations included, but were not limited to, habitus, color of urine, color and consistency of feces (dry, normal, soft, diarrhea, blood in feces), salivation, vomiting, skin lesions and an obvious change in general condition..."

b. Clinical assessments: From information on pages 23-24 of MRID 49788722 there were two pre-application clinical examinations on days -14 and -3 (±2). From p. 24: "These examinations included, but were not limited to, vital signs (pulse rate, respiratory rate and rectal temperatures), mucous membranes, eyes, motility, lymph nodes, abdominal palpation, thoracic auscultation and skin condition." There is no indication that there was any clinical examination following application of the control/test material.

c. Application site observations: After treatment, the application site was observed twice daily for changes to the skin and fur. Any erythema/eschar and edema were scored according to the Draize scale, and the presence or absence of cosmetic changes to the hair, spiking (hair coming together in narrow, sharp points) and deposits (areas of test item visible on the surface), were also recorded.

2. Body weight: The puppies were weighed on days -3 ± 2, -1, 7, 14, 29. 37 and 44.

3. Food consumption: The amounts of food offered daily to each dog and approximate percentages of offered food consumed were recorded for days -14 through +43.

4. Clinical pathology: On days -14 or -13, 1, 7, 31 and 37 blood for hematology, clinical chemistry, and coagulation evaluation was collected.

The CHECKED (X) parameters were examined.

a. Hematology:

X	Hematocrit (HCT)*	X	Leukocyte differential count* (absolute and percentages)
X	Hemoglobin (HGB)*	X	Mean corpuscular HGB (MCH)*
X	Leukocyte count (WBC)*	X	Mean corpusc. HGB conc.(MCHC)*
X	Erythrocyte count (RBC)*	X	Mean corpusc. volume (MCV)*
	Platelet count		Reticulocyte count
	Blood clotting measurements		Morphology (if indicated)
X	(Activated Partial Thromboplastin time) (aPTT)*		Heinz body formation
	(Clotting time)		
X	\(Prothrombin time) (PT)*		

* Recommended for companion animals safety evaluation based on the 870.7200 Guidelines.

b. Clinical chemistry:

	ELECTROLYTES		OTHER
X	Calcium*	X	Albumin*
X	Chloride*	X	Creatinine*
	Magnesium		Urea nitrogen (BUN)*
X	Phosphorus*		Cholesterol
X	Potassium*		Globulins*
X	Sodium*	X	Glucose*
	ENZYMES	X	Total bilirubin*
X	Alkaline phosphatase (ALK)*	X	Direct bilirubin*
	Cholinesterase (ChE)**	X	Indirect (or conjugated) bilirubin
	Creatinine phosphokinase	X	Total protein (TP)*
	Lactic acid dehydrogenase (LDH)		Triglycerides
X	Alanine aminotransferase (ALT/also SGPT)*		Serum protein electrophoresis
X	Aspartate aminotransferase (AST/also SGOT)*	X	Albumin/globulin ratio
	Sorbitol dehydrogenase	X	Urea
	Gamma glutamyl transferase (GGT)		
	Glutamate dehydrogenase		

* Recommended for a companion animal safety evaluation based on the 870.7200 Guidelines.
** Only recommended if one or more active ingredients in the formulation is a known cholinesterase inhibitor.

Reference ranges (associated with out-of-range values) are provided for hematology (pages 38, 80-91 of MRID 49788722) and clinical chemistry (pages 34-35 and 92-103 of MRID 49788722).

5. **Urinalysis:** Urinalysis is not required for companion animal safety studies and was not done as part of the current study.

6. **Sacrifice and pathology:** There were no deaths or moribund sacrifices during the study. Terminal sacrifices and gross necropsies were not done and are not required under OPPTS 870.7200.

II. RESULTS

B. OBSERVATIONS:

1. Clinical signs:

The following pre-exposure observations are reported on p. 31 of MRID 49788722:

Group	Day	Animal IDs	Observation
1	-7	698 0C0	Blood in faeces; faecal float negative
	-6 to -2		Lack of appetite
	-1		Improved
4	-11	578 202	Blood in faeces (watery)
	-10		Improved
	-7	5C3 CC8	Blood in faeces; faecal float negative
	-6		Blood in faeces
	-5		Improved
	-6 to -4	5A7 EOO	Loose faeces

The following post-exposure observations are reported on p. 30 of MRID 49788722:

Group 1			Group 4		
Day	Animal ID	All signs observed	Day	Animal ID	All signs observed
2	698 0C0	Coughing	1	5A2 CBA	Slight inappetance
4		Coughing	1	5A7 EOO	Listless; diarrhoea
5		Coughing	13	5A7 D8F	Loose faeces; listless
7	5A6 6BA	Loose faeces	14		Loose faeces
8		Loose faeces; bilateral eye discharge	19		Listless
9		Eye discharge – left	27, 28	5A7 EOO	Diarrhoea
14	698 27F	Loose faeces	37	5A4 2FD	Diarrhoea
15, 19		Diarrhoea			
26	5A6 AAC	Eye discharge			
27		Lacrimation			
40	698 27F	Diarrhoea			
39 - 44	5A6 6BA	Eye discharge			
Group 1: Dogs received the Control Substance Group 4: Dogs received the Test Substance (T2), at five times the recommended dose					

There is no indication in the post-exposure observations given above of any patterns consistent with toxicity from the test substance at 5X the recommended dose. From

information on pages 40-42 of MRID 49788722 three group 1 puppies and nine group 4 puppies received medications for coccidia prophylaxis after day 0.

2. **Food consumption:**

Individual daily food consumption values are reported on pages 1382 to 1441 of MRID 49788722. The initial daily ration was 0.5 cup/day/puppy. This was increased to 0.75 cup/day/puppy for 7 Group 1 and 7 Group 4 puppies on day 33 or 36.

Group 4 puppy 5A2 CBA is reported (p. 30 of MRID 49788722) as having slight inappetance on Day 1. From p. 1415 of MRID 49788722 this puppy consumed 0-25% of its ration on day 0 and 75-100% on day 1.

The following occurrences of individual daily food consumption values ranging from 0-25% are reported on pages 1382 to 1441 of MRID 49788722:

Group 1:

5A4 191 (M) Days -14, -13, -8, 5, 9
5A6 004 (F) Day -13
5A6 AAC (M) Days -13, -9, -4, 13
5B3 DA9 (M) Days -12, -11, -10, -8
697 FFA (F) Days -13, -12, 0, 1, 36
698 0C0 (F) Days -13, -12, -8, -7, -6, -2, -1, 1
698 27F (M) Days -14, -13, -12

Group 4:

5A2 CBA (F) Days -13, -8, -2, 0, 10
5A3 1B0 (M) Days -13, -12, -11
5A4 2FD (M) Days -14, -13, -12, -11, 11
5A5 8B9 (M) Day -9
5A7 D8F (M) Days -14, -12, 9, 18
5A7 E00 (F) Days -12, -11, -8, -6, -1, 0, 6
5A8 8F3 (F) Days -12, 40
5C3 CC8 (F) Day -11
5D1 0EA (F) Day -11

The puppies were evidently under stress (separation from the dam?) at the start of acclimation. Although two Group 4 puppies (5A2 CBA and 5A7 E00) had 0-25% food consumption on day 0 this was temporary (from p. 1415 of MRID 49788722 5A2 CBA had 75-100% food consumption on days 1 and 2, and from p. 1427 5A7 E00 had 25-50% consumption on day 2 and 50-75% on day 3).

From p. 58 of MRID 49788722: "Food consumption was inconsistent in both groups from Day -13 to Day -1. In group 1, more than 90% of the puppies consumed >75% to 100% of their prescribed amount of food (according to manufacturer's recommendations) on Day 0, compared with 75% in group 4. From Days 1 to 21, the percentage of puppies in group 1 who ate >75% to 100% of their food ranged from 41.7% to 91.7%, and was similar to group 4, which ranged from 50% to 100%. Both groups showed a steady improvement in food consumption during the 24-day period from Day 21 to Day 44. During that period in group 1, >75% to 100% food consumption was observed in 100% of the puppies on seven days, in >90% of the puppies on six days, in >80% of the puppies on 10 days and in >:70% of the puppies on one day. During that same [24-day] period in group 4, >75% to 100% food consumption was observed in 100% of the puppies on 12 days and in >90% of the puppies on 12 days... Based on...[these] observations, the groups did not differ with regard to food consumption from Day -13 to Day 20, and group 4 showed better food consumption from Day 21 to Day 44."

3. **Body weight and weight gain:**

The following means and standard deviations are calculated from individual body weight as reported on pages 1375 through 1380 of MRID 49788722.

Mean Body Weights (in kg) by Group and Sex						
	Day -1	Day 7	Day 14	Day 29	Day 37	Day 44
Group 1:						
Males	2.07 ± 0.69	2.45 ± 0.75	2.83 ± 0.90	3.96 ± 1.24	4.30 ± 1.24	4.79 ± 1.23
Females	1.82 ± 0.54	2.16 ± 0.71	2.59 ± 0.94	3.48 ± 1.25	4.01 ± 1.40	4.29 ± 1.44
Combined	1.94 ± 0.61	2.30 ± 0.72	2.71 ± 0.89	3.72 ± 1.22	4.16 ± 1.27	4.54 ± 1.31
Group 4:						
Males	2.25 ± 0.31	2.68 ± 0.31	3.07 ± 0.48	4.23 ± 0.69	4.77 ± 0.69	5.12 ± 0.68
Females	2.22 ± 0.77	2.57 ± 0.89	3.12 ± 0.97	4.08 ± 1.26	4.50 ± 1.18	4.99 ± 1.29
Combined	2.24 ± 0.56	2.62 ± 0.63	3.09 ± 0.73	4.15 ± 0.97	4.63 ± 0.93	5.06 ± 0.98

Mean Body Weight Gains (in kg) by Group and Sex					
	Day -1 to 7	Day 7 to 14	Day 14 to 29	Day 29 to 44	Day -1 to 44
Group 1:					
Males	0.38 ± 0.19	0.38 ± 0.20	1.12 ± 0.35	0.83 ± 0.10	2.72 ± 0.62
Females	0.34 ± 0.21	0.43 ± 0.23	0.90 ± 0.35	0.81 ± 0.27	2.47 ± 0.96
Combined	0.36 ± 0.18	0.41 ± 0.21	1.01 ± 0.35	0.82 ± 0.19	2.59 ± 0.78
Group 4:					
Males	0.43 ± 0.09	0.39 ± 0.24	1.16 ± 0.29	0.90 ± 0.22	2.88 ± 0.46
Females	0.35 ± 0.18	0.55 ± 0.15	0.96 ± 0.32	0.92 ± 0.20	2.77 ± 0.53
Combined	0.39 ± 0.14	0.47 ± 0.21	1.06 ± 0.31	0.91 ± 0.20	2.82 ± 0.48

From information on p. 1376 the mean weight of the four lowest weight male and four lowest weight female Group 4 puppies on day -1 was 1.96 ± 0.46 kg (4.32 ± 1.01 lb), so the study supports a minimum body weight of 5.00 lbs (rounding up from 4.32 lb).

Calculating individual doses (in mL/kg) for Group 4 puppies on Day 30 gives the following:

Females:

57B 202	1.0183
5A2 CBA	0.6452
5A7 B00	0.8811
5A8 8F3	0.5391
5C3 CC8	0.9025
5D1 0EA	1.0121

Males:

5A3 1B0	0.9804
5A4 2FD	0.5900
5A5 8B9	0.4474
5A7 D8F	0.5882
5BB 58F	0.4484
697 E35	0.4415

The mean of the 4 highest female values and 4 highest male values is 0.8026 mL/kg. Dividing this by 5 gives 0.1605 mL/kg, which is equivalent to 0.0729 mL/lb. The minimum weight associated with a 0.4 mL application supported by the 30-day data is then 0.4 mL ÷ 0.0729 mL/lb = 5.49 lb.

The minimum weight supported by the day 0 dosages is 5.00 lbs (rounded up from the 4.32 lbs obtained from the Day -1 bodyweights).

The following are the body weight statistics from p. 32 of MRID 49788722:

Group	Statistic	Baseline (Day -1)	Day 44	Change (Day 44)	%Change (Day 44)
1	n	12	12	12	12
	Mean	1.944	4.538	2.594	135.199
	SD	0.606	1.307	0.780	25.987
	Median	1.965	4.770	2.510	132.441
	Minimum	1.080	2.220	1.140	103.140
	Maximum	3.270	6.840	3.630	178.820
4	n	12	12	12	12
	Mean	2.235	5.058	2.823	131.011
	SD	0.561	0.982	0.480	26.550
	Median	2.235	5.320	2.750	125.018
	Minimum	1.100	3.300	2.200	103.170
	Maximum	3.140	6.790	3.650	200.000

Group 1: Negative control
Group 4: Dogs were treated topically with five times the dose of T2

The following are the p values associated with a comparison of bodyweights from Groups 1 and 4 (from p. 32 of MRID 49788722):

		p-values				
Parameter	Comparison	Day 7	Day 14	Day 29	Day 37	Day 44
Weight (kg)	4 - 1	0.6719	0.4497	0.5484	0.4650	0.3973

Group 1: Negative control
Group 4: Dogs were treated topically with five times the dose of T2

Overall there are no indications of any effect on bodyweights or bodyweight gains.

4. <u>Local effects at the application site</u>:

Incidences of "local" (application site?) effects are reported on pages 115-161 of MRID 49788722. Only cosmetic effects were observed, with the following incidences at 1 and 2 hours following application on Day 1 (from p. 115 of MRID 49788722):

Day	Time	Abnormality	Group 1	Group 4
0	1h	Spiking (wet paint brush effect)	12/12 (100.0%)	12/12 (100.0%)
	1h	Deposit on tips of hair	9/12 (75.00%)	12/12 (100.0%)
	1h	Greasy appearance	12/12 (100.0%)	9/12 (75.00%)
	1h	Slight scaling	0/12	0/12
	1h	Scales (>2mm x 2mm)	0/12	0/12
	1h	Pruritus (itching and scratching)	0/12	0/12
	1h	Very slight erythema (barely perceptible)	0/12	0/12
	1h	Other	0/12	0/12
0	2h	Spiking (wet paint brush effect)	12/12 (100.0%)	12/12 (100.0%)
	2h	Deposit on tips of hair	11/12 (91.67%)	12/12 (100.0%)
	2h	Greasy appearance	12/12 (100.0%)	9/12 (75.00%)
	2h	Slight scaling	0/12	0/12
	2h	Scales (>2mm x 2mm)	0/12	0/12
	2h	Pruritus (itching and scratching)	0/12	0/12
	2h	Very slight erythema (barely perceptible)	0/12	0/12
	2h	Other	0/12	0/12

Group 1: Control Substance group
Group 4: Dogs were treated topically with five times the dose of T2

The following incidences of cosmetic effects were observed on Day 1 (from p. 117 of MRID 49788722):

Day	Time	Abnormality	Group 1	Group 4
1	obs1	Spiking (wet paint brush effect)	8/12 (66.67%)	6/12 (50.00%)
	obs1	Deposit on tips of hair	6/12 (50.00%)	10/12 (83.33%)
	obs1	Greasy appearance	10/12 (83.33%)	2/12 (16.67%)
	obs1	Slight scaling	2/12 (16.67%)	6/12 (50.00%)
	obs1	Scales (>2mm x 2mm)	0/12	0/12
	obs1	Pruritus (itching and scratching)	0/12	0/12
	obs1	Very slight erythema (barely perceptible)	0/12	0/12
	obs1	Other	0/12	0/12
1	obs2	Spiking (wet paint brush effect)	7/12 (58.33%)	6/12 (50.00%)
	obs2	Deposit on tips of hair	6/12 (50.00%)	8/12 (66.67%)
	obs2	Greasy appearance	8/12 (66.67%)	2/12 (16.67%)
	obs2	Slight scaling	5/12 (41.67%)	6/12 (50.00%)
	obs2	Scales (>2mm x 2mm)	0/12	0/12
	obs2	Pruritus (itching and scratching)	0/12	0/12
	obs2	Very slight erythema (barely perceptible)	0/12	0/12
	obs2	Other	0/12	0/12

Group 1: Control Substance group
Group 4: Dogs were treated topically with five times the dose of T2

The following cosmetic effects were still present on Day 29 (from p. 145 of MRID 49788722):

Day	Time	Abnormality	Group 1	Group 4
29	obs1	Spiking (wet paint brush effect)	0/12	0/12
	obs1	Deposit on tips of hair	0/12	0/12
	obs1	Greasy appearance	0/12	0/12
	obs1	Slight scaling	3/12 (25.00%)	3/12 (25.00%)
	obs1	Scales (>2mm x 2mm)	0/12	1/12 (8.33%)
	obs1	Pruritus (itching and scratching)	0/12	0/12
	obs1	Very slight erythema (barely perceptible)	0/12	0/12
	obs1	Other	0/12	0/12
29	obs2	Spiking (wet paint brush effect)	0/12	0/12
	obs2	Deposit on tips of hair	0/12	0/12
	obs2	Greasy appearance	0/12	0/12
	obs2	Slight scaling	3/12 (25.00%)	3/12 (25.00%)
	obs2	Scales (>2mm x 2mm)	0/12	1/12 (8.33%)
	obs2	Pruritus (itching and scratching)	0/12	0/12
	obs2	Very slight erythema (barely perceptible)	0/12	0/12
	obs2	Other	0/12	0/12

Group 1: Control Substance group
Group 4: Dogs were treated topically with five times the dose of T2

All day 0 to day 44 incidences of pruritus (itching and scratching) and very slight erythema (barely perceptible) are reported as 0/12 for both Groups 1 and 2.

5. **Mortality:** There were no deaths or moribund sacrifices.

C. BLOOD ANALYSES:

1. Hematology and coagulation parameters:

The "most obvious" (p. 37 of MRID 49788722) individual out-of-range hematology parameter values are reported on p. 38 of MRID 49788722:

Parameter	Reference range	Animal ID	Day	Value recorded
Group 1				
White cell count (x10^9/L)	(10 - 23.6)	698 0C0	1	51.1
White cell count (x10^9/L)	(10 - 23.6)	698 0C0	7	48
Neutrophils Abs (x10^9/L)	(3.8 - 13.83)	698 0C0	1	28.16
Neutrophils Abs (x10^9/L)	(3.8 - 13.83)	698 0C0	7	33.94
Lymphocytes Abs (x10^9/L)	(4.21 - 7.95)	5B3 DA9	1	10.03
Lymphocytes Abs (x10^9/L)	(4.21 - 7.95)	698 0C0	1	17.63
Lymphocytes Abs (x10^9/L)	(4.21 - 7.95)	698 0C0	7	10.66
Lymphocytes Abs (x10^9/L)	(4.21 - 7.95)	698 27F	31	10.52
Monocytes Abs (x10^9/L)	(0.88 - 2.15)	698 27F	7	3.01
Eosinophils Abs (x10^9/L)	(0.1 - 0.57)	698 0C0	1	1.94
Basophils Abs (x10^9/L)	(0.02 - 0.11)	698 0C0	1	0.56
Basophils Abs (x10^9/L)	(0.02 - 0.11)	698 0C0	7	0.29
Platelet count (x10^9/L)	(249 - 847)	5A4 191	1	185
Platelet count (x10^9/L)	(249 - 847)	5A4 191	7	124
Platelet count (x10^9/L)	(249 - 847)	5A6 004	7	148
Prothrombin time (sec)	(5.8 - 46.7)	697 FFA	31	95.7
Patient aPTT (sec)	(10.1 - 17.2)	5A9 67F	31	23.1
Group 4				
Neutrophils Abs (x10^9/L)	(3.8 - 13.83)	5A7 E00	1	18.6
Prothrombin time (sec)	(5.8 - 46.7)	5A8 8F3	7	73.2
Prothrombin time (sec)	(5.8 - 46.7)	5A8 8F3	31	77.8
Prothrombin time (sec)	(5.8 - 46.7)	697 E35	7	66.1
Prothrombin time (sec)	(5.8 - 46.7)	697 E35	31	80.6

Group 1: Negative control
Group 4: Dogs were treated topically with five times the dose of T2

None of the above findings were considered to be clinically relevant.

Two Group 4 puppies had aPTT values that were below the reference range on day 1. On p. 37 of MRID 49788722 it is stated that the value for 5C3 CC8 could be a result of a gastrointestinal inflammation during the study, but that for 5D1 0EA was not accompanied by any clinical signs. From p. 57 of MRID 49788722:

Parameter	Animal ID	Group	Reference range	Day	Base value	End value	Change from baseline
Patient PTT (sec)	5C3 CC8	4	10.1 - 17.2	1	10.6	8.1	-2.5
	5D1 0EA	4	10.1 - 17.2	1	10.7	9.9	-0.8

Group 1: Control Substance group
Group 4: Dogs were treated topically with five times the dose of T2

It is stated (p. 37 of MRID 49788722) that: "The haematology results were not indicative of any test item related condition."

2. **Clinical chemistry:**

The "most obvious" (p. 33 of MRID 49788722) individual out-of-range clinical chemistry parameter values are reported on p. 34 (Group 1) and 35 (Group 4) of MRID 49788722. For Group 1:

Group	Parameter	Reference range	Animal ID	Day	Value recorded
1	Urea-S (mmol/L)	(2 - 4.9)	5A6 004	37	6.2
		(2 - 4.9)	5A6 6BA	1	6.3
		(2 - 4.9)	5A6 6BA	37	6.5
		(2 - 4.9)	697 FFA	31	6.5
		(2 - 4.9)	698 0C0	1	6.2
	Creatinine-S (umol/L)	(15 - 37)	5A3 923	1	55
		(15 - 37)	5A6 004	1	51
		(15 - 37)	5A6 6BA	1	59
		(15 - 37)	5A6 6BA	7	53
		(15 - 37)	5A6 004	37	51
		(15 - 37)	697 FFA	31	57
		(15 - 37)	698 27F	7	54
	Alk. phosphatase-S (u/L)	(108 - 198)	5A4 191	1	232
		(108 - 198)	5B2 F7C	1	240
		(108 - 198)	5B2 F7C	7	235
		(108 - 198)	5B2 F7C	31	256
		(108 - 198)	5B2 F7C	37	256
		(108 - 198)	698 27F	1	259
	ALT (SGPT) (u/L)	(10 - 33)	698 0C0	1	52
	AST (SGOT) (u/L)	(12 - 41)	5B2 F7C	1	55
		(12 - 41)	698 27F	37	66

Group 1: Negative control

For Group 4:

Group	Parameter	Reference range	Animal ID	Day	Value recorded
4	Urea-S (mmol/L)	(2 - 4.9)	57B 202	37	6.4
		(2 - 4.9)	5A2 CBA	1	6.3
		(2 - 4.9)	5A7 E00	1	6.1
		(2 - 4.9)	5A7 E00	31	7.5
	Creatinine-S (umol/L)	(15 - 37)	5A4 2FD	1	53
		(15 - 37)	5A7 E00	31	67
		(15 - 37)	5A7 E00	37	55
		(15 - 37)	5A8 8F3	1	53
	Bilirubin total-S (umol/L)	(2 - 3)	5A2 CBA	37	6
	Alk. phosphatase-S (u/L)	(108 - 198)	5A3 1B0	1	245
		(108 - 198)	5A3 1B0	7	228
		(108 - 198)	5A3 1B0	31	230
		(108 - 198)	5A3 1B0	37	236
		(108 - 198)	5D1 0EA	1	252

Group 4: Dogs were treated topically with five times the dose of T2

From p. 33 of MRID 49788722: "The clinical chemistry results were not indicative of any test item related condition."

A. **INVESTIGATORS' CONCLUSIONS:** The study author concluded [p. 8 of MRID 49788722] that: "The Test Substance T2, containing imidacloprid, permethrin and pyriproxyfen, administered twice within a 30-day interval at 5x the recommended dose was safe to use under the conditions of the study. An adequate margin of safety was indicated between the control group and the 5X dose as there were no toxic signs recorded in any of these groups."

B. **REVIEWER'S COMMENTS:** This reviewer is in agreement with the stated conclusions of the study author with respect to the lack of toxicity that occurred in beagle puppies at 5x the recommended dose. In addition, the proposed minimum age of 7 weeks is supported by this study. However, the proposed label dosages and weight bands are not entirely supported by this study.

According to the proposed label dosages are 0.014 fl. oz. (0.4 mL) for 4-10 lb dogs; 0.034 fl. oz. (1.0 mL) for 11-20 lb dogs; 0.084 fl. oz. (2.5 mL) for 21-55 lb dogs; and 0.135 fl. oz. (4.0 mL) for dogs 55 lbs and over. The maximum dosages associated with these four respective weight bands would then be 0.1 mL/lb, 0.091 mL/lb; 0.119 mL/lb, and 0.073 mL/lb.

The proposed minimum weight on the label of 91384-G is 4 lbs. From information on p. 1376 the mean weight of the four lowest weight male and four lowest weight female Group 4 (5X) puppies on day -1 was 1.96 ± 0.46 kg (4.33 ± 1.01 lb), so the 5X dosage rate was 1.02 mL/kg (0.46 mL/lb). [From information on p. 1375 the mean weight of the four lowest weight male and four lowest weight female Group 1 puppies was 1.63 ± 0.38 kg (3.60 ± 0.84 lbs), so that lower weight puppies were available]. The mean 5X application rate of 1.02 mL/kg (0.46 mL/lb) supports a 1X application rate of 0.204 mL/kg or 0.0926 mL/lb. Rounding up from 4.33 lbs, it is concluded that the minimum weight supported by this study for a dosage of 0.4 mL is 5 lbs, and that the minimum weight associated with a 2.5 mL dosage is 27 lbs. The labeling should be revised accordingly, or the registrant should provide additional information (such as the amount of dosage actually dispensed by an applicator) justifying the proposed dosages and associated weight ranges.

This companion animal safety study in puppies (beagles) is **Acceptable** with the dosage rate revisions indicated above. It **does satisfy** the guideline requirement for a companion animal safety study (OPPTS 870.7200) in 7-week old puppies.

C. **STUDY DEFICIENCIES:** As indicated above, because the mean weight of the four lowest weight male and four lowest female Group 4 (5X) puppies on day -1 was 1.96 kg (4.33 lb), the study does not support a minimum weight of 4 lbs. In order to support a 4 lb minimum weight claim, the mean weight of these eight puppies would have had to have been 1.81 kg.

The following is the Acute Toxicity Data Evaluation Record (DER) for 7-week beagle puppy safety study conducted on T2, Batch No. T2MD06 and submitted for EPA File Symbol 91384-G.

1. DP BARCODE: 432710				
2. PC CODES: 129099 (Imidacloprid: 8.71%); 109701 (Permethrin: 44.97%); 129032 (Pyriproxyfen: 0.43%)				
3. CURRENT DATE: July 27, 2016				
4. TEST MATERIAL: T2, Batch No. T2MD06; containing (p. 21 of MRID 49788722) Imidacloprid: 8.71% w/w; Permethrin: 44.97% w/w; and Pyriproxyfen: 0.43% w/w. In an acute oral LD_{50} study (p. 15 of MRID 49788715) with the same batch number (T2MD06) the test material is described as a liquid with a specific gravity of 1.144.				
Study/Species/Lab Study # /Date	**MRID**	**Results**	**Tox Cat**	**Core Grade**
Companion animal safety / dog (7-week old beagle puppies) / Clin Vet International, Bloemfontein, South Africa / Project No. CV/15/155, PN1767/ December 3, 2015 / OCSPP 870.7200 Companion animal safety / dog adult beagle (Report Supplement) / Clin Vet International, Bloemfontein, South Africa / Project No. CV/15/155, PN1767/ March 18, 2016/ OCSPP 870.7200	49788722 49866902	2 groups, each consisting of 6M & 6F beagle puppies (49-51 days old at the start of the study), 1.08-3.27 kg on day -1. Puppies were treated on Days 0 & 30. Group 1 (controls) were treated with a 5x dose of mineral oil and Group 4 (5X) received a 5X dose of test material. Study went to Day 44. Since all Group 4 puppies weighed 1.08-3.27 kg on day -1 they were all dosed with 5 x 0.4 mL test substance on Day 0. On Day 30 four group 4 puppies (4.91-5.54 kg on day 29) were dosed with 5 x 1.0 mL test substance; other 8 with 5 x 0.4 mL. Daily observations (both groups) showed occurrences of loose feces, eye discharge and diarrhea. One group 4 puppy had slight inappetance on day 1 and another had diarrhea and was listless on day 1. Both had recovered by day 2. There were no indications of any test material related effects on food consumption, body weights, or body weight gains. No indications of any dose-related effects on hematology or clinical chemistry parameters. Only cosmetic effects (spiking, greasiness, deposits on tips of hair) were observed, with no pruritus and/or erythema. Mean weight of 4 lowest weight males & 4 lowest females on day -1 was 1.96 kg so study supports dosage rate of 0.4 mL/1.96 kg = 0.4 mL/4.32 lbs. Rounding up would be 5 lbs, which is the minimum weight associated with 0.4 mL.	N/A	A with label revision

n.d. = not determined; Core Grade Key: A =Acceptable, S = Supplementary, W = Waived, U = Unacceptable, D = Data Gap

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

To: Elizabeth Fertich

From: Tim Ciarlo, MS, Entomologist

Secondary Review: Jennifer Saunders, Ph.D., Acting Senior Entomologist

Date: July 27, 2016

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD (DER)

[redacted]

Note: MRIDs found to be **unacceptable** to support label claims should be removed from the data matrix.

DP barcode: 431031
Decision no.: 511951
Submission no: 978275
Action code: R315
Product Name: T2.200 for Dogs
EPA Reg. No or File Symbol: 91384-G
Formulation Type: Spot-On for Dogs
Ingredients statement from the label with PC codes included:

Permethrin	44%	PC: 109701
Imidacloprid	8.8%	PC: 129099
Pyriproxyfen	0.44%	PC: 129032

Application rate(s) of product and each active ingredient (lbs. or gallons/1000 square feet or per acre as appropriate; and g/m^2 or mg/cm^2 or mg/kg body weight as appropriate): The proposed label assigns 4 different sizes according to a dog's body weight. For 4-10 lb (1.81-4.54 kg) dogs, a 0.4 ml dose is indicated. For 11-20 lb (4.99-9.07 kg) dogs, a 1.0 ml dose is indicated. For 21-55 lb (9.53-24.95 kg) dogs, a 2.5 ml dose is indicated. For dogs over 55 lbs (24.95 kg), a 4.0 ml dose is indicated. Active ingredient doses are identified below. Ninety pounds was used as the upper end of the largest weight range, despite the label not giving an upper limit.

Body Weight Class	Amount of Product Applied	Active Ingredient Doses (mg/kg)*
4-10 lbs or 1.81-4.54 kg	0.4 ml (0.46 g)	Imidacloprid – 22.35 to 8.94 (at 10 lbs) Permethrin – 111.17 to 44.70 (at 10 lbs) Pyriproxyfen – 1.18 to 0.45 (at 10 lbs)
11-20 lbs or 4.99-9.07 kg	1.0 ml (1.152 g)	Imidacloprid – 20.31 to 11.17 (at 20 lbs) Permethrin – 101.58 to 55.86 (at 20 lbs) Pyriproxyfen – 1.06 to 0.56 (at 20 lbs)
21-55 lbs or 9.53-24.95 kg	2.5 ml (2.88 g)	Imidacloprid – 26.61 to 10.16 (at 55 lbs) Permethrin – 133.04 to 50.79 (at 55 lbs) Pyriproxyfen – 1.33 to 0.51 (at 55 lbs)

>55 lbs or >24.95 kg	4.0 ml (4.608)	Imidacloprid – 16.25 to 9.93 (at 90 lbs) Permethrin – 81.27 to 49.67 (at 90 lbs) Pyriproxyfen – 0.81 to 0.50 (at 90 lbs)

*Based on a product density of 1.152 g/ml and active ingredient concentrations listed above.

Imidacloprid dosages are: 8.94 mg/kg to 26.61 mg/kg
Permethrin dosages are: 44.70 mg/kg to 133.04 mg/kg
Pyriproxyfen dosages are: 0.45 mg/kg to 1.33 mg/kg

Use Patterns: Monthly spot-on insecticide for dogs, applied to the skin between the dog's shoulder blades. For dogs weighing 4-10 lbs and 11-20 lbs, apply product to one spot. For dogs weighing 21-55 lbs and over 55 lbs, apply product in 3 or 4 spots on the top of the back of the dog from the shoulder to the base of the tail.

I. Action Requested: The registrant has submitted 12 MRIDs to support the registration of a new spot-on insecticide for dogs. The Risk Manager has requested review of these MRIDs to determine if the efficacy claims sought are adequately supported.

II. Background: This product was submitted to the Agency for registration 12/3/2016. None of the submitted MRIDs have been previously reviewed by the Agency.

III. MRID Summary (Primary Reviews Attached, Except for MRID 49788712):

49788701. Erasmus, H. (2015) A Pilot Study to Assess the Local Tolerance and Efficacy of T2 Formulation against ticks (*Rhipicephalus sanguineus*) and Fleas (*Ctenocephalides felis*) on Dogs Final Report. Project Number: CV/15/143. Unpublished study prepared by ClinVet International (Pty) Ltd. 95p.

(1) GLP

(2) **Methods:** This study evaluated the efficacy of T2 formulation against brown dog ticks (*Rhipicephalus sanguineus*) and cat fleas (*Ctenocephalides felis*) when applied topically to dogs. T2 formulation contains the same active ingredients at the same concentrations as the subject product and is therefore an appropriate test sample. Eight dogs (equal numbers male/female) were divided into two groups, each containing 4 dogs. Group 1 served as the untreated control group, while dogs in Group 2 were treated with a spot-on application of T2. Of the 4 dogs in Group 2, 3 ranged in weight from 12-18.8 kg and received a 2.5 ml dose, while 1 weighed 23.5 kg and received a 4.0 ml dose. Group 1 dogs ranged in weight from 9.9-22.7 kg.

The test substance was administered to Group 2 dogs on day 0. Dogs weighing 9-25 kg received the application in 3 spots, while dogs weighing >22.5 kg received the application in 4 spots. All dogs were acclimatized beginning on day -7. Approximately 100 *C. felis* fleas were introduced to each animal on days -7 and 28. Fifty *R. sanguineus* ticks were introduced to each animal on day 28. Fleas were counted and removed on days -5 and 30. Ticks were counted and removed on day 30. Geometric means as well as arithmetic means of flea and tick counts were reported. Percent efficacy was calculated for both fleas and ticks with the following formula:

Percent Efficacy = 100 x $(M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean number of live fleas/ticks (free, attached, or engorged) on dogs in the untreated control group.

M_t = Geometric or arithmetic mean number of live fleas/ticks (free, attached, or engorged) on dogs in the T2 treatment group.

(3) **Results:** Mean tick counts on day 30 in the Group 1 untreated control dogs were reported as 31.2 and 32.0 using geometric and arithmetic means, respectively. In the T2 treated dogs, these figures were 2.8 and 6.8. Percent efficacy was reported as 91% when using geometric means, and 78.9% when using arithmetic means.

Mean flea counts on day 30 in the Group 1 untreated control dogs were reported as 77.4 and 78.3 using geometric and arithmetic means, respectively. In the T2 treated dogs, these figures were 1.7 and 12.5. Percent efficacy was reported as 97.8% when using geometric means, and 84.0% when using arithmetic means.

(4) **Conclusion: Unacceptable.** This pilot study only included 4 dogs per treatment group. A minimum of 6 dogs per treatment group should be used. In addition, percent efficacy against both brown dog ticks and cat fleas exceeded 90% when using geometric means, but not when using arithmetic means. Percent efficacy on day 30 against ticks and fleas 48 hours after infestation was reported as 78.9% and 84.0%, respectively, when using arithmetic means. The Agency prefers the use of arithmetic means for efficacy studies that rely on count data, as is the case here. Geometric means are more appropriate for continuous data that follow a log-normal distribution. Moreover, efficacy should be assessed at either 24 or 48 hours after treatment, and then weekly through 4 weeks. Efficacy was only assessed here on day 30, so there is no way to know if the product is efficacious between days 0 and 30. Additionally, the dog weighing 23.5 kg was given a 4.0 ml dose of T2, when it should have been 2.5 ml per the proposed label.

49788702. Liebenberg, J. (2015) A Dose Confirmation of T2 Formulation against Artificial Infestations of Adult Ticks (*Ixodes scapularis*) on Dogs Final Report. Project Number: CV/15/144, PN1767. Unpublished study prepared by ClinVet International (Pty) Ltd. 107p.

(1) GLP

(2) **Methods:** This study evaluated the efficacy of T2 formulation (Batch number T2MD04) against blacklegged ticks (*Ixodes scapularis*) when applied topically to dogs. T2 formulation contains the same active ingredients as the subject product, but at slightly different concentrations (8.67% imidacloprid, 45.21% permethrin, and 0.42% pyriproxyfen). Sixteen dogs (equal numbers male/female) were divided into two groups, each containing 8 dogs. Dogs in Group 1 served as the control group and were treated with mineral oil, while dogs in Group 2 were treated with a spot-on application of T2. The 8 dogs in Group 2 ranged in weight from 16.7-20.5 kg (average weight of 18.38 kg) and received a 2.5 ml dose of T2. Of the dogs in Group 1, 7 ranged in weight from 14.5-22.1 kg and received a 2.5 ml dose of mineral oil, while 1 dog weighed 26.8 kg and received a 4.0 ml dose of mineral oil.

The test substance or mineral oil was administered to dogs on day 0. Dogs weighing 9-25 kg received the application in 3 spots, while dogs weighing >25 kg received the application in 4 spots. The doses for each dog in Group 2 have been calculated and are as follows:

Dog's weight (kg)	Amount of T2 applied (ml)	Dose of imidacloprid (mg/kg)*	Dose of permethrin (mg/kg)*	Dose of pyriproxyfen (mg/kg)*
16.86	2.5	14.81	77.23	0.72
20.22	2.5	12.35	64.39	0.60
18.52	2.5	13.48	70.31	0.65
17.46	2.5	14.30	74.57	0.69
16.73	2.5	14.93	77.83	0.72
18.38	2.5	13.59	70.84	0.66
20.47	2.5	12.20	63.61	0.59
18.39	2.5	13.58	70.80	0.66
Averages				
18.38	2.5	13.59	70.84	0.66

* A density of 1.152 g/ml was assumed

All dogs were acclimatized beginning on day -7. One-hundred adult *Ix. scapularis* ticks (50 males, 50 females) were introduced to each animal on days -7, -2, 7, 14, 21, and 28. Ticks were counted and removed on days –5, 2, 9, 16, 23, and 30 (48 hours ± 2 hours post-infestation or test substance administration). Geometric means as well as arithmetic means of tick counts were reported. Percent efficacy was calculated on each day ticks were counted and removed with the following formula:

Percent Efficacy = 100 x $(M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean number of live ticks (free, attached, or engorged) on dogs in the untreated control group.

M_t = Geometric or arithmetic mean number of live ticks (free, attached, or engorged) plus dead engorged ticks on dogs in the T2 treatment group.

(3) **Results:** Only female *Ix. scapularis* ticks feed on dogs, so data collection was limited to female ticks. Tick counts at the time points tested are summarized below using geometric means:

Day	Group 1 Mean (Control)	Group 2 Mean (Treatment)	Percent Efficacy
2	31.4	13.0	58.6
9	30.0	0.0	**100.0**
16	35.2	0.0	**100.0**
23	33.2	0.0	**100.0**
30	35.7	0.0	**100.0**

Tick counts at the time points tested are summarized below using arithmetic means:

Day	Group 1 Mean (Control)	Group 2 Mean (Treatment)	Percent Efficacy
2	32.5	18.5	43.1
9	30.5	0.0	**100.0**
16	35.6	0.0	**100.0**
23	33.5	0.0	**100.0**
30	36.0	0.0	**100.0**

Percent efficacy on Day 2 was reported as 58.6% when using geometric means, and 43.1% when using arithmetic means. On all other days ticks were counted, percent efficacy was reported as 100% regardless of whether geometric or arithmetic means were used. The tables above contain percent efficacy figures for each tick count day. Values >90% are bolded.

(4) **Conclusion: Unacceptable.** This study shows that a 2.5 ml dose of the subject product kills blacklegged (*Ix. scapularis*) ticks for up to 30 days on dogs weighing up to 18.38 kg (40.52 lbs), although adequate efficacy was not achieved until 9 days after the test substance was applied. Assuming a density of 1.152 g/ml, this equates to an average of 13.59 mg imidacloprid/kg, 70.84 mg permethrin/kg, and 0.66 mg pyriproxyfen/kg. The proposed label suggests 2.5 ml should be applied to dogs weighing 9.53-24.95 kg. A 24.95 kg dog would receive 10.5 mg imidacloprid/kg, 50.79 mg permethrin/kg, and 0.51 mg pyriproxyfen/kg. Because the tested rates exceed the labeled rates for dogs weighing 9.53-24.95 kg, this study **cannot support any** efficacy claims. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg). Efficacy should also be demonstrated before 9 days post test substance administration.

49788703. de Vos, C. (2015) A Dose Confirmation of T2 Formulation against Artificial Infestations of Ticks (*Dermacentor variabilis*) on Dogs Final Report. Project Number: CV/15/145, PN1767. Unpublished study prepared by ClinVet International (Pty) Ltd. 93p.

(1) GLP

(2) **Methods:** This study evaluated the efficacy of T2 formulation (Batch number T2MD04) against American dog ticks (*Dermacentor variabilis*) when applied topically to dogs. T2 formulation contains the same active ingredients as the subject product, but at slightly different concentrations (8.67% imidacloprid, 45.21% permethrin, and 0.42% pyriproxyfen). Sixteen dogs were divided into two groups, each containing 8 dogs (6 males/2 females). Dogs in

Group 1 served as the control group and were treated with mineral oil, while dogs in Group 2 were treated with a spot-on application of T2. The 8 dogs in Group 2 ranged in weight from 12.60-23.60 kg (average weight of 16.85 kg) and received a 2.5 ml dose of T2. Of the dogs in Group 1, 1 weighed 7.80 kg and received a 1.0 ml dose of mineral oil, 6 ranged in weight from 13.80-19.00 kg and received a 2.5 ml dose of mineral oil, and 1 dog weighed 25.20 kg and received a 4.0 ml dose of mineral oil.

The test substance or mineral oil was administered to dogs on day 0. Dogs weighing 9-25 kg received the application in 3 spots. The doses for each dog in Group 2 have been calculated and are as follows:

Dog's weight (kg)	Amount of T2 applied (ml)	Dose of imidacloprid (mg/kg)*	Dose of permethrin (mg/kg)*	Dose of pyriproxyfen (mg/kg)*
12.60	2.5	19.2	103.34	0.96
19.00	2.5	13.12	68.53	0.64
15.60	2.5	16.01	83.46	0.78
23.60	2.5	10.58	55.17	0.51
14.20	2.5	17.58	91.69	0.85
20.80	2.5	12.00	62.60	0.58
14.40	2.5	17.34	90.42	0.84
14.60	2.5	17.10	89.18	0.83
Averages				
16.85	2.5	15.37	80.55	0.75

* A density of 1.152 g/ml was assumed

All dogs were acclimatized beginning on day -7. Fifty adult *D. variabilis* ticks (balanced sex ratio) were introduced to each animal on days -7, -2, 7, 14, 21, and 28. Ticks were counted and removed on days –5, 2, 9, 16, 23, and 30 (48 hours ± 2 hours post-infestation or test substance administration). Geometric means as well as arithmetic means of tick counts were reported. Percent efficacy was calculated on each day ticks were counted and removed with the following formula:

Percent Efficacy = 100 x $(M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean number of live ticks (free, attached, or engorged) on dogs in the untreated control group.

M_t = Geometric or arithmetic mean number of live ticks (free, attached, or engorged) plus dead engorged ticks on dogs in the T2 treatment group.

(3) **Results:** Tick counts at the time points tested are summarized below using geometric means:

Day	Group 1 Mean (Control)	Group 2 Mean (Treatment)	Percent Efficacy
2	17.9	17.0	5.2
9	14.6	0.0	**100.0**
16	16.3	0.1	**99.4**
23	15.6	0.1	**99.1**
30	16.5	0.4	**97.8**

Tick counts at the time points tested are summarized below using arithmetic means:

Day	Group 1 Mean (Control)	Group 2 Mean (Treatment)	Percent Efficacy
2	19.8	18.4	7.0
9	17.0	0.0	**100.0**
16	17.1	0.1	**99.3**
23	16.0	0.3	**98.4**

30	17.9	0.6	**96.5**

Percent efficacy on Day 2 was reported as 5.2% when using geometric means, and 7.0% when using arithmetic means. On all other days ticks were counted, percent efficacy was reported as >90% regardless of whether geometric or arithmetic means were used. The tables above contain percent efficacy figures for each tick count day. Values >90% are bolded.

(4) **Conclusion: Unacceptable.** This study shows that a 2.5 ml dose of the subject product kills American dog (*D. variabilis*) ticks for up to 30 days on dogs weighing up to 16.85 kg (37.15 lbs), although adequate efficacy was not achieved until 9 days after the test substance was applied. Assuming a density of 1.152 g/ml, this equates to an average of 15.37 mg imidacloprid/kg, 80.55 mg permethrin/kg, and 0.75 mg pyriproxyfen/kg. The proposed label suggests 2.5 ml should be applied to dogs weighing 9.53-24.95 kg. A 24.95 kg dog would receive 10.5 mg imidacloprid/kg, 50.79 mg permethrin/kg, and 0.51 mg pyriproxyfen/kg. Because the tested rates exceed the labeled rates for dogs weighing 9.53-24.95 kg, this study **cannot support any** efficacy claims. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg). Efficacy should also be demonstrated before 9 days post test substance administration.

49788704. Neethling, W. (2015) A Dose Confirmation of T2 Formulation against Artificial Infestations of Ticks (*Rhipicephalus sanguineus*) and Fleas (*Ctenocephalides felis*) on Dogs Final Report. Project Number: CV/15/146, PN1767. Upublished study prepared by ClinVet International (Pty) Ltd. 117p.

(1) GLP

(2) **Methods:** This study evaluated the efficacy of T2 formulation (Batch number T2MD04) against brown dog ticks (*Rhipicephalus sanguineus*) and cat fleas (*Ctenocephalides felis*) when applied topically to dogs. T2 formulation contains the same active ingredients as the subject product, but at slightly different concentrations (8.67% imidacloprid, 45.21% permethrin, and 0.42% pyriproxyfen). Sixteen dogs were divided into two groups, each containing 8 dogs (7 males/1 female). Dogs in Group 1 served as the control group and were treated with mineral oil, while dogs in Group 2 were treated with a spot-on application of T2. The 8 dogs in Group 2 ranged in weight from 14.8-25.0 kg (average weight of 18.68 kg) and received a 2.5 ml dose of T2. The 8 dogs in Group 1 ranged in weight from 14.6-22.6 kg (average weight of 17.63 kg) and received a 2.5 ml dose of mineral oil.

The test substance or mineral oil was administered to dogs on day 0. Dogs weighing 9-25 kg received the application in 3 spots. The doses for each dog in Group 2 have been calculated and are as follows:

Dog's weight (kg)	Amount of T2 applied (ml)	Dose of imidacloprid (mg/kg)*	Dose of permethrin (mg/kg)*	Dose of pyriproxyfen (mg/kg)*
22.2	2.5	11.25	58.65	0.55
18.8	2.5	13.28	69.26	0.64
16.8	2.5	14.86	77.50	0.72
14.8	2.5	16.87	87.98	0.82
16.4	2.5	15.23	79.39	0.74
17.2	2.5	14.52	75.70	0.70
25.0	2.5	9.99	52.08	0.48
18.2	2.5	13.72	71.54	0.66
Averages				
18.68	2.5	13.71	71.51	0.66

* A density of 1.152 g/ml was assumed

All dogs were acclimatized beginning on day -7. Fifty adult *R. sanguineus* ticks (balanced sex ratio) were introduced to each animal on days -2, 7, 14, 21, and 28. Approximately 100 *C. felis* fleas were introduced to each animal on days -7, -2, 7, 14, 21, and 28. Ticks were counted and removed on days 2, 9, 16, 23, and 30 (48 hours ± 2

hours post-infestation or test substance administration). Fleas were counted and removed on days -5, 2, 9, 16, 23, and 30. Geometric means as well as arithmetic means of both flea and tick counts were reported. Percent efficacy was calculated on each day fleas and ticks were counted and removed with the following formula:

Percent Efficacy = 100 x $(M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean number of live fleas/ticks (free, attached, or engorged) on dogs in the untreated control group.

M_t = Geometric or arithmetic mean number of live fleas/ticks (free, attached, or engorged) plus dead engorged ticks on dogs in the T2 treatment group.

(3) **Results:** Tick counts at the time points tested are summarized below using geometric means:

Day	Group 1 Mean (Control)	Group 2 Mean (Treatment)	Percent Efficacy
2	20.5	19.8	3.4
9	18.4	0.2	**99.0**
16	26.8	0.5	**98.2**
23	23.5	0.0	**100.0**
30	26.2	1.4	**94.6**

Tick counts at the time points tested are summarized below using arithmetic means:

Day	Group 1 Mean (Control)	Group 2 Mean (Treatment)	Percent Efficacy
2	21.6	21.0	2.9
9	20.5	0.3	**98.8**
16	28.3	0.6	**97.8**
23	24.4	0.0	**100.0**
30	27.5	2.0	**92.7**

Percent efficacy on Day 2 was reported as 3.4% when using geometric means, and 2.9% when using arithmetic means. On all other days ticks were counted, percent efficacy was reported as >90% regardless of whether geometric or arithmetic means were used. The tables above contain percent efficacy figures for each tick count day. Values >90% are bolded.

Flea counts at the time points tested are summarized below using geometric means:

Day	Group 1 Mean (Control)	Group 2 Mean (Treatment)	Percent Efficacy
2	53.3	0.0	**100.0**
9	82.9	0.0	**100.0**
16	84.6	0.1	**99.9**
23	83.8	0.0	**100.0**
30	85.8	0.3	**99.7**

Flea counts at the time points tested are summarized below using arithmetic means:

Day	Group 1 Mean (Control)	Group 2 Mean (Treatment)	Percent Efficacy
2	55.3	0.0	**100.0**
9	83.8	0.0	**100.0**
16	85.3	0.1	**99.9**
23	84.9	0.0	**100.0**
30	86.4	0.6	**99.3**

On all days fleas were counted, percent efficacy was reported as >90% regardless of whether geometric or

arithmetic means were used. The tables above contain percent efficacy figures for each flea count day. Values >90% are bolded.

(4) **Conclusion: Unacceptable.** This study shows that a 2.5 ml dose of the subject product kills brown dog (*R. sanguineus*) ticks and cat fleas (*R. sanguineus*) for up to 30 days on dogs weighing up to 18.68 kg (41.18 lbs), although adequate efficacy was not achieved against ticks until 9 days after the test substance was applied. Assuming a density of 1.152 g/ml, this equates to an average of 13.71 mg imidacloprid/kg, 71.51 mg permethrin/kg, and 0.66 mg pyriproxyfen/kg. The proposed label suggests 2.5 ml should be applied to dogs weighing 9.53-24.95 kg. A 24.95 kg dog would receive 10.5 mg imidacloprid/kg, 50.79 mg permethrin/kg, and 0.51 mg pyriproxyfen/kg. Because the tested rates exceed the labeled rates for dogs weighing 9.53-24.95 kg, this study **cannot support any** efficacy claims. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg). Efficacy should also be demonstrated before 9 days post test substance administration.

49788705. Liebenberg, J. (2015) A Dose Confirmation of T2 Formulation against Artificial Infestations of Ticks (*Amblymomma americanum*) on Dogs Final Report. Project Number: CV/15/147, PN1767. Unpublished study prepared by ClinVet International (Pty) Ltd. 101p.

(1) GLP

(2) **Methods:** This study evaluated the efficacy of T2 formulation (Batch number T2MD06) against lone star ticks (*Amblyomma americanum*) when applied topically to dogs. T2 formulation contains the same active ingredients as the subject product, but at slightly different concentrations (8.71% imidacloprid, 44.97% permethrin, and 0.43% pyriproxyfen). Sixteen dogs were divided into two groups, each containing 8 dogs (6 males/2 females). Dogs in Group 1 served as the control group and were treated with mineral oil, while dogs in Group 2 were treated with a spot-on application of T2. The 8 dogs in Group 2 ranged in weight from 15.4-23.0 kg (average weight of 19.48 kg) and received a 2.5 ml dose of T2. The 8 dogs in Group 1 ranged in weight from 16.4-21.0 kg (average weight of 19.15 kg) and received a 2.5 ml dose of mineral oil.

The test substance or mineral oil was administered to dogs on day 0. Dogs weighing 9-25 kg received the application in 3 spots. The doses for each dog in Group 2 have been calculated and are as follows:

Dog's weight (kg)	Amount of T2 applied (ml)	Dose of imidacloprid (mg/kg)*	Dose of permethrin (mg/kg)*	Dose of pyriproxyfen (mg/kg)*
16.6	2.5	15.11	78.02	0.75
19.6	2.5	12.80	66.08	0.63
17.8	2.5	14.09	72.76	0.70
23	2.5	10.91	56.31	0.54
19.8	2.5	12.67	65.41	0.63
21.2	2.5	11.83	61.09	0.58
15.4	2.5	16.29	84.10	0.80
22.4	2.5	11.20	57.82	0.55
Averages				
19.48	2.5	13.11	67.70	0.65

* A density of 1.152 g/ml was assumed

All dogs were acclimatized beginning on day -7. Thirty adult *A. americanum* ticks (balanced sex ratio) were introduced to each animal on days -4, -2, 7, 21, and 28. Ticks were counted and removed on days –2, 2, 9, 23, and 30 (48 hours ± 2 hours post-infestation or test substance administration). Geometric means as well as arithmetic means of tick counts were reported. Percent efficacy was calculated on each day ticks were counted and removed with the following formula:

Percent Efficacy = 100 x $(M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean number of live ticks (free, attached, or engorged) on dogs in the untreated control group.

M_t = Geometric or arithmetic mean number of live ticks (free, attached, or engorged) plus dead engorged ticks on dogs in the T2 treatment group.

(3) **Results:** Tick counts at the time points tested are summarized below using geometric means:

Day	Group 1 Mean (Control)	Group 2 Mean (Treatment)	Percent Efficacy
2	14.2	12.3	13.5
9	16.1	0.4	**97.7**
23	19.6	1.1	**94.2**
30	17.8	1.2	**93.4**

Tick counts at the time points tested are summarized below using arithmetic means:

Day	Group 1 Mean (Control)	Group 2 Mean (Treatment)	Percent Efficacy
2	14.5	13.4	7.8
9	16.3	0.6	**96.2**
23	20.0	2.4	88.1
30	17.9	2.3	87.4

Percent efficacy on Day 2 was reported as 13.5% when using geometric means, and 7.8% when using arithmetic means. On all other days ticks were counted, percent efficacy was reported as >90% when geometric means were used. When arithmetic means were used, >90% efficacy was only achieved on Day 9 (reported as 96.2%). The tables above contain percent efficacy figures for each tick count day. Values >90% are bolded.

(4) **Conclusion: Unacceptable.** This study shows that a 2.5 ml dose of the subject product kills lone star (*A. americanum*) ticks for up to 9 days on dogs weighing up to 19.48 kg (42.95 lbs), although adequate efficacy was not achieved until 9 days after the test substance was applied. Assuming a density of 1.152 g/ml, this equates to an average of 13.11 mg imidacloprid/kg, 67.70 mg permethrin/kg, and 0.65 mg pyriproxyfen/kg. The proposed label suggests 2.5 ml should be applied to dogs weighing 9.53-24.95 kg. A 24.95 kg dog would receive 10.5 mg imidacloprid/kg, 50.79 mg permethrin/kg, and 0.51 mg pyriproxyfen/kg. Because the tested rates exceed the labeled rates for dogs weighing 9.53-24.95 kg, this study **cannot support any** efficacy claims. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg). Efficacy figures beyond 9 days did not reach 90% and therefore do not support efficacy claims. The Agency prefers the use of arithmetic means for efficacy studies that rely on count data, as is the case here. Geometric means are more appropriate for continuous data that follow a log-normal distribution. Efficacy should also be demonstrated before 9 days post test substance administration.

49788706. Neethling, W. (2015) A Dose Confimation of the Efficacy of T2 Formulation against Mosquitoes on Dogs Experimentally Exposed to *Aedes aegypti* Final Report. Project Number: CV/15/148, PN1767. Unpublished Study Prepared by ClinVet International (Pty) Ltd. 130p.

(1) GLP

(2) **Methods:** This study evaluated the efficacy of T2 formulation (Batch number T2MD01) against *Aedes aegypti* mosquitoes when applied topically to dogs. T2 formulation contains the same active ingredients as the subject product, but at slightly different concentrations (8.7% imidacloprid, 45.17% permethrin, and 0.42% pyriproxyfen). Sixteen dogs were divided into two groups, each containing 8 dogs (4 males/4 females in Group 1; 5 males/3 females in Group 2). Dogs in Group 1 served as the control group and were treated with mineral oil, while dogs in

Group 2 were treated with a spot-on application of T2. Of the dogs in Group 1, 1 weighed 8.2 kg and received a 1.0 ml dose of mineral oil, 5 ranged in weight from 11.4-23.4 kg and received a 2.5 ml dose of mineral oil, and 2 dogs weighed 25.2 and 27.6 kg and received a 4.0 ml dose of mineral oil. Of the dogs in Group 2, 7 ranged in weight from 11.4-24.8 kg and received a 2.5 ml dose of T2, and 1 dog weighed 26.0 kg and received a 4.0 ml dose of T2.

The test substance or mineral oil was administered to dogs on day 0. Dogs weighing up to 9 kg received the application in 2 spots. Dogs weighing 9-25 kg received the application in 3 spots. Dogs weighing >25 kg received the application in 4 spots. The doses for each dog in Group 2 have been calculated and are as follows:

Dog's weight (kg)	Amount of T2 applied (ml)	Dose of imidacloprid (mg/kg)*	Dose of permethrin (mg/kg)*	Dose of pyriproxyfen (mg/kg)*
11.6	2.5	21.60	112.15	1.04
17.8	2.5	14.08	73.08	0.68
11.4	2.5	21.98	114.11	1.06
12.0	2.5	20.88	108.41	1.01
22.2	2.5	11.29	58.60	0.55
26.0	4.0	15.42	80.06	0.74
24.8	2.5	10.10	52.46	0.49
22.0	2.5	11.39	59.13	0.55
Averages				
18.48	--	15.84	82.25	0.76

* A density of 1.152 g/ml was assumed

All dogs were acclimatized beginning on day -7. All dogs were challenged with approximately 50 adult female *Ae. aegypti* mosquitoes on days -5, 1, 7, 14, 21, and 28. Dogs were sedated and placed in a mosquito-proof cage (81 cm x 58 cm x 58 cm) with the mosquitoes for a duration of 1 hour. The number of mosquitoes exhibiting probing behavior in a manner indicative of a blood feeding attempt was recorded at the end of the 1 hour challenge period. At the conclusion of each challenge period, mosquitoes were assessed as living, moribund, or dead and transferred to clean containers (if alive/moribund) for 24 hour mortality determinations. Dead mosquitoes were squashed to determine if blood feeding had occurred. After the 24 hour post-challenge period, all mosquitoes were squashed to determine if blood feeding had occurred. Because final mosquito viability assessments were conducted 24 hours after each challenge period, results are reported for days 2, 8, 15, 22, and 29.

Four outcomes were investigated: killing effect, knockdown, anti-feeding effect, and repellency. Both geometric and arithmetic means were reported. Each outcome calculation is described below:

Killing Effect (% Efficacy) = $100 \times (M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean percentage of live and moribund mosquitoes (fed and unfed) in the control group at 24 hours post challenge.

M_t = Geometric or arithmetic mean percentage of live and moribund mosquitoes (fed and unfed) in the T2 treatment group at 24 hours post challenge.

Knockdown Effect (% Efficacy) = $100 \times (M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean percentage of live mosquitoes (fed and unfed) in the control group at the conclusion of the 1 hour challenge period.

M_t = Geometric or arithmetic mean percentage of live mosquitoes (fed and unfed) in the T2 treatment group at the conclusion of the 1 hour challenge period.

Anti-feeding Effect (% Efficacy) = $100 \times (M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean percentage of the cumulative number of mosquitoes that successfully took a blood meal (includes live, moribund, and dead individuals) in the control group at 60 minutes and 24 hours post challenge.

M_t = Geometric or arithmetic mean percentage of the cumulative number of mosquitoes that successfully took a blood meal (includes live, moribund, and dead individuals) in the T2 treatment group at 60 minutes and 24 hours post challenge.

Repellency (% Efficacy) = 100 x $(M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean number of probing incidents in the control group at the conclusion of the 1 hour challenge period.

M_t = Geometric or arithmetic mean number of probing incidents in the T2 treatment group at the conclusion of the 1 hour challenge period.

(3) **Results:** Killing effect at the time points tested are summarized below using geometric means:

Day	Group 1 % Living + Moribund (Control)	Group 2 % Living + Moribund (Treatment)	Percent Efficacy
2	96.1	8.5	**91.1**
8	86.8	3.9	**95.5**
15	86.8	0.6	**99.3**
22	96.4	28.7	70.2
29	79.1	2.9	**96.4**

Killing effect at the time points tested are summarized below using arithmetic means:

Day	Group 1 % Living + Moribund (Control)	Group 2 % Living + Moribund (Treatment)	Percent Efficacy
2	96.2	17.7	81.6
8	87.6	7.3	**91.7**
15	87.2	1.1	**98.7**
22	96.5	32.6	66.2
29	79.7	4.9	**93.8**

Percent efficacy on Day 2 was reported as 91.1% when using geometric means, and 81.6% when using arithmetic means. After Day 2, percent efficacy was reported as >90% at all other time points killing effect was investigated with the exception of Day 22 (70.2% efficacy with geometric means; 66.2% efficacy with arithmetic means). This was true for calculations involving both arithmetic and geometric means. The tables above contain percent efficacy figures for each killing effect assessment day. Values >90% are bolded.

Knockdown effect at the time points tested are summarized below using geometric means:

Day	Group 1 % Living (Control)	Group 2 % Living (Treatment)	Percent Efficacy
2	98.9	38.6	60.9
8	99.7	12.8	87.2
15	98.2	12.2	87.5
22	100.0	32.2	67.8
29	98.3	21.1	78.5

Knockdown effect at the time points tested are summarized below using arithmetic means:

Day	Group 1 % Living (Control)	Group 2 % Living (Treatment)	Percent Efficacy
2	98.9	48.4	51.1
8	99.7	17.4	82.5
15	98.2	21.3	78.3
22	100.0	35.9	64.1
29	98.3	24.0	75.6

Percent efficacy after the 1 hour challenge period on all days knockdown was assessed was reported as <90% when using both geometric and arithmetic means. The tables above contain percent efficacy figures for each knockdown effect assessment day. Values >90% are bolded.

Anti-feeding effect at the time points tested are summarized below using geometric means:

Day	Group 1 % Blood Fed (Control)	Group 2 % Blood Fed (Treatment)	Percent Efficacy
2	39.7	0.4	**99.0**
8	90.8	4.1	**94.9**
15	33.3	2.5	**92.5**
22	30.6	2.0	**93.5**
29	74.0	4.6	**93.8**

Anti-feeding effect at the time points tested are summarized below using arithmetic means:

Day	Group 1 % Blood Fed (Control)	Group 2 % Blood Fed (Treatment)	Percent Efficacy
2	55.5	0.7	**98.8**
8	82.8	6.2	**92.5**
15	38.2	3.7	**90.4**
22	31.6	3.3	89.6
29	74.7	6.5	91.3

A >90% reduction in blood feeding on T2 treated dogs was reported for each anti-feeding effect assessment day, regardless of whether geometric or arithmetic means were used. Percent efficacy on Day 22 was 89.6 and is reasonably close to 90%. The tables above contain percent efficacy figures for each anti-feeding effect assessment day. Values >90% are bolded.

Repellency effect at the time points tested are summarized below using geometric means:

Day	Group 1 Probing Incidents (Control)	Group 2 Probing Incidents (Treatment)	Percent Efficacy
1	76.5	9.0	88.2
7	103.5	11.2	89.2
14	61.9	7.5	87.9
21	65.8	9.4	85.8
28	84.6	29.6	65.0

Repellency effect at the time points tested are summarized below using arithmetic means:

Day	Group 1 Probing Incidents (Control)	Group 2 Probing Incidents (Treatment)	Percent Efficacy
1	78.0	9.8	87.5

7	112.3	13.5	88.0
14	65.3	7.9	87.9
21	67.6	10.3	84.8
28	87.6	29.8	66.0

Percent efficacy after the 1 hour challenge period on all days repellency was assessed was reported as <90% when using both geometric and arithmetic means. The tables above contain percent efficacy figures for each repellency effect assessment day. Values >90% are bolded.

(4) **Conclusion: Unacceptable.** This study **does not** support that the subject product kills *Ae. aegypti* mosquitoes on dogs weighing up to 18.48 kg (40.74 lbs) at application rates of 15.84 mg imidacloprid/kg, 82.25 mg permethrin/kg, and 0.76 mg pyriproxyfen/kg (assuming a density of 1.152 g/ml). Although greater than 90% of mosquitoes exposed to T2 treated dogs were killed 8 and 15 days after the test substance was applied, mortality dipped to an unacceptably low 66% 22 days after test substance administration. Efficacy did recover to 94% on day 29. However, because the tested rates exceed the proposed labeled rates, this study **cannot support any** efficacy claims unless the upper bounds of the proposed label dose rates are adjusted accordingly. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg).

This study **does not** support that the subject product knocks down *Ae. aegypti* mosquitoes at the tested rates mentioned above. At no time point did percent knockdown exceed 90% in mosquitoes exposed to T2 treated dogs. Knockdown should also be demonstrated within 30 seconds of exposure to an insecticidal treatment. The Agency prefers the use of arithmetic means for efficacy studies that rely on count data, as is the case here. Geometric means are more appropriate for continuous data that follow a log-normal distribution.

This study shows that the subject product elicits an anti-feeding effect in *Ae. aegypti* mosquitoes for up to 29 days on dogs weighing up to 18.48 kg (40.74 lbs) at application rates of 15.84 mg imidacloprid/kg, 82.25 mg permethrin/kg, and 0.76 mg pyriproxyfen/kg (assuming a density of 1.152 g/ml). A >90% reduction in blood feeding on T2 treated dogs was reported for each anti-feeding effect assessment day, regardless of whether geometric or arithmetic means were used. Percent efficacy on Day 22 was 89.6 and is reasonably close to 90%. However, because the tested rates exceed the proposed labeled rates, this study **cannot support any** efficacy claims. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg).

This study **does not** support that the subject product repels *Ae. aegypti* mosquitoes at the tested rates mentioned above. At no time point did percent repellency exceed 90% in mosquitoes exposed to T2 treated dogs. The Agency prefers the use of arithmetic means for efficacy studies that rely on count data, as is the case here. Geometric means are more appropriate for continuous data that follow a log-normal distribution.

This study **does not** support general mosquito claims. Representative species from the genera *Culex*, *Aedes*, and *Anopheles* should be tested for a general mosquito claim. The Agency's rationale for this is that these three genera encompass most of the important disease vectors in the United States. In addition, the average consumer is unable to distinguish an *Aedes* species, let alone *Ae. aegypti* from other mosquitoes.

49788707. de Vos, C. (2015) A Dose Confirmation of T2 Formulation against Artificial Infestations of Stable Flies (*Stomoxys calcitrans*) and Onset of Efficacy of T2 Formulation against Fleas (*Ctenocephalides felis*) on Dogs Final Report. Project Number: CV/15/149, PN1767. Unpublished study prepared by ClinVet International (Pty) Ltd. 182p.

(1) GLP

(2) **Methods:** This study evaluated the efficacy of T2 formulation (Batch number T2MD06) against stable flies (*Stomoxys calcitrans*) when applied topically to dogs. Onset of efficacy against cat fleas (*Ctenocephalides felis*) was investigated as a secondary objective. T2 formulation contains the same active ingredients as the subject product,

but at slightly different concentrations (8.71% imidacloprid, 44.97% permethrin, and 0.43% pyriproxyfen). Fourteen dogs were divided into two groups, each containing 7 dogs (4 males/3 females in Group 1; 5 males/2 females in Group 2). Dogs in Group 1 served as the control group and were treated with mineral oil, while dogs in Group 2 were treated with a spot-on application of T2. Of the dogs in Group 1, 6 ranged in weight from 10.45-20.82 kg and received a 2.5 ml dose of mineral oil, and 1 dog weighed 25.77 kg and received a 4.0 ml dose of mineral oil. Of the dogs in Group 2, 6 ranged in weight from 14.09-20.90 kg and received a 2.5 ml dose of T2, and 1 dog weighed 25.29 kg and received a 4.0 ml dose of T2.

The test substance or mineral oil was administered to dogs on day 0. Dogs weighing 9-25 kg received the application in 3 spots. Dogs weighing >25 kg received the application in 4 spots. The doses for each dog in Group 2 have been calculated and are as follows:

Dog's weight (kg)	Amount of T2 applied (ml)	Dose of imidacloprid (mg/kg)*	Dose of permethrin (mg/kg)*	Dose of pyriproxyfen (mg/kg)*
14.09	2.5	17.80	91.92	0.88
16.77	2.5	14.96	77.23	0.74
15.80	2.5	15.88	81.97	0.78
25.29	4.0	15.87	81.94	0.78
19.62	2.5	12.79	66.01	0.63
20.58	2.5	12.19	62.93	0.60
20.90	2.5	12.00	61.97	0.59
Averages				
19.01	--	14.50	74.85	0.72

* A density of 1.152 g/ml was assumed

All dogs were acclimatized beginning on day -7. All dogs were challenged with approximately 20 adult stable flies on days 1, 7, 14, 21, and 28. Dogs were sedated and placed in a fly-proof cage (81 cm x 58 cm x 58 cm) with the stable flies for a duration of 1 hour. The number of stable flies exhibiting probing behavior in a manner indicative of a blood feeding attempt was recorded at the end of the 1 hour challenge period. At the conclusion of each challenge period, stable flies were assessed as living, moribund, or dead and transferred to clean containers (if alive/moribund) for 24 hour mortality determinations. After the 24 hour post-challenge period, all flies were squashed (abdomens only) to determine if blood feeding had occurred. Final stable fly viability assessments were conducted 24 hours after each challenge period.

Four stable fly outcomes were investigated: killing effect, knockdown, anti-feeding effect, and repellency. Both geometric and arithmetic means were reported. Each outcome calculation is described below:

Killing Effect (% Efficacy) = 100 x $(M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean cumulative percentage of live and moribund stable flies (fed and unfed) in the control group at 24 hours post challenge.

M_t = Geometric or arithmetic mean cumulative percentage of live and moribund stable flies (fed and unfed) in the T2 treatment group at 24 hours post challenge.

Knockdown Effect (% Efficacy) = 100 x $(M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean cumulative percentage of live stable flies (fed and unfed) in the control group at the conclusion of the 1 hour challenge period.

M_t = Geometric or arithmetic mean cumulative percentage of live stable flies (fed and unfed) in the T2 treatment group at the conclusion of the 1 hour challenge period.

Anti-feeding Effect (% Efficacy) = 100 x $(M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean cumulative percentage of stable flies that successfully took a blood meal (includes live, moribund, and dead individuals) in the control group at 60 minutes and 24 hours post challenge.

M_t = Geometric or arithmetic mean cumulative percentage of stable flies that successfully took a blood meal (includes live, moribund, and dead individuals) in the T2 treatment group at 60 minutes and 24 hours post challenge.

Repellency (% Efficacy) = 100 x $(M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean number of probing incidents in the control group at the conclusion of the 1 hour challenge period.

M_t = Geometric or arithmetic mean number of probing incidents in the T2 treatment group at the conclusion of the 1 hour challenge period.

The same dogs were also challenged with 100 adult cat fleas (*C. felis*) on Day 0, 12 hours after test substance administration to investigate the killing effect against fleas. Fleas were introduced to the skin of each animal on Days -7 and -2. Live fleas on each animal were combed out and counted on Days -5 and 0.

(3) **Results:** Killing effect at 24 hours after fly challenge are summarized below using geometric means:

Day	Group 1 % Living + Moribund (Control)	Group 2 % Living + Moribund (Treatment)	Percent Efficacy
1	29.8	0.5	**98.2**
7	11.9	0.0	**100.0**
14	5.9	0.0	**100.0**
21	17.7	0.7	**96.2**
28	1.7	0.0	**100.0**

Killing effect at 24 hours after fly challenge are summarized below using arithmetic means:

Day	Group 1 % Living + Moribund (Control)	Group 2 % Living + Moribund (Treatment)	Percent Efficacy
1	39.3	2.9	**92.7**
7	21.8	0.0	**100.0**
14	13.0	0.0	**100.0**
21	33.4	1.4	**95.7**
28	5.8	0.0	**100.0**

Percent efficacy on all days killing effect was tested was reported as >90% when using both geometric and arithmetic means. However, control mortality was unacceptably high at all time points. Control mortality should not exceed 10%. The tables above contain percent efficacy figures for each killing effect assessment day. Values >90% are bolded.

Knockdown effect at 1, 2, 4, and 8 hours after fly challenge are summarized below using geometric means:

Day	Group 1 % Living (Control)	Group 2 % Living (Treatment)	Percent Efficacy
Day 1 (1 hour)	50.2	0.5	**98.9**
Day 7 (1 hour)	41.8	0.3	**99.3**
Day 7 (2 hours)	24.9	0.0	**100.0**
Day 7 (4 hours)	19.8	0.0	**100.0**
Day 7 (8 hours)	14.7	0.0	**100.0**

Day 14 (1 hours)	31.6	0.0	**100.0**
Day 14 (2 hours)	24.2	0.0	**100.0**
Day 14 (4 hours)	15.6	0.0	**100.0**
Day 14 (8 hours)	9.9	0.0	**100.0**
Day 21 (1 hour)	68.3	1.7	**97.5**
Day 21 (2 hours)	46.4	0.9	**98.0**
Day 21 (4 hours)	39.6	0.8	**97.9**
Day 21 (8 hours)	30.0	0.3	**99.0**
Day 28 (1 hour)	66.4	0.4	**99.4**
Day 28 (2 hours)	5.8	0.4	**93.0**
Day 28 (4 hours)	4.2	0.0	**100.0**
Day 28 (8 hours)	2.1	0.0	**100.0**

Knockdown effect at 1, 2, 4, 8, and 24 hours after fly challenge are summarized below using arithmetic means:

Day	Group 1 % Living (Control)	Group 2 % Living (Treatment)	Percent Efficacy
Day 1 (1 hour)	62.9	2.9	**95.5**
Day 1 (24 hours)	35.7	2.9	**92.0**
Day 7 (1 hour)	54.3	0.8	**98.6**
Day 7 (2 hours)	45.8	0.0	**100.0**
Day 7 (4 hours)	36.8	0.0	**100.0**
Day 7 (8 hours)	27.6	0.0	**100.0**
Day 7 (24 hours)	21.8	0.0	**100.0**
Day 14 (1 hours)	62.2	0.0	**100.0**
Day 14 (2 hours)	44.1	0.0	**100.0**
Day 14 (4 hours)	30.0	0.0	**100.0**
Day 14 (8 hours)	15.9	0.0	**100.0**
Day 14 (24 hours)	12.3	0.0	**100.0**
Day 21 (1 hour)	71.9	4.3	**94.0**
Day 21 (2 hours)	59.5	2.9	**95.2**
Day 21 (4 hours)	51.7	2.1	**95.9**
Day 21 (8 hours)	44.6	0.7	**98.4**
Day 21 (24 hours)	31.0	1.4	**95.4**
Day 28 (1 hour)	70.6	1.4	**98.0**
Day 28 (2 hours)	10.1	1.4	85.9
Day 28 (4 hours)	7.3	0.0	**100.0**
Day 28 (8 hours)	5.8	0.0	**100.0**
Day 28 (24 hours)	1.4	0.0	**100.0**

Percent efficacy at each time point after the 1 hour challenge period on all days knockdown was assessed was >90% when using both geometric and arithmetic means, except for 85.9% efficacy on Day 28, 2 hours after the challenge period (arithmetic means). However, control mortality was unacceptably high at all time points. Control mortality should not exceed 10%. The tables above contain percent efficacy figures for each knockdown effect assessment day. Values >90% are bolded.

Anti-feeding effect at the time points tested are summarized below using geometric means:

Day	Group 1 % Blood Fed (Control)	Group 2 % Blood Fed (Treatment)	Percent Efficacy
1	20.3	0.7	**96.8**
7	10.6	0.0	**100.0**
14	11.5	0.0	**100.0**

21	14.2	0.0	**100.0**
28	49.4	0.7	**98.6**

Anti-feeding effect at the time points tested are summarized below using arithmetic means:

Day	Group 1 % Blood Fed (Control)	Group 2 % Blood Fed (Treatment)	Percent Efficacy
1	24.3	1.4	**94.3**
7	14.7	0.0	**100.0**
14	26.2	0.0	**100.0**
21	21.7	0.0	**100.0**
28	51.7	1.4	**97.2**

A >90% reduction in blood feeding on T2 treated dogs was reported for each anti-feeding effect assessment day, regardless of whether geometric or arithmetic means were used. The tables above contain percent efficacy figures for each anti-feeding effect assessment day. Values >90% are bolded.

Repellency effect at the time points tested are summarized below using geometric means:

Day	Group 1 Probing Incidents (Control)	Group 2 Probing Incidents (Treatment)	Percent Efficacy
1	8.2	0.0	**100.0**
7	3.0	0.0	**100.0**
14	1.9	0.0	**100.0**
21	4.1	0.0	**100.0**
28	9.7	0.0	**100.0**

Repellency effect at the time points tested are summarized below using arithmetic means:

Day	Group 1 Probing Incidents (Control)	Group 2 Probing Incidents (Treatment)	Percent Efficacy
1	8.3	0.0	**100.0**
7	4.1	0.0	**100.0**
14	2.4	0.0	**100.0**
21	4.9	0.0	**100.0**
28	10.7	0.0	**100.0**

Percent efficacy after the 1 hour challenge period on all days repellency was assessed was reported as 100% regardless of whether geometric or arithmetic means were used. The tables above contain percent efficacy figures for each repellency effect assessment day. Values >90% are bolded.

Killing effect against fleas 12 hours after test substance administration are summarized below:

Day	Group 1 % of Fleas on Animal (Control)	Group 2 % of Fleas on Animal (Treatment)	Percent Efficacy
0 (geometric means)	89.6	0.5	**99.4**
0 (arithmetic means)	91.6	1.4	**98.4**

Percent efficacy 12 hours after test substance administration was reported as >90% regardless of whether geometric or arithmetic means were used. The number of live fleas recovered from dogs in Group 1 is sufficient for this part of the study to support the subject product. The tables above contain percent efficacy figures for Day 0. Values >90% are bolded.

(4) **Conclusion: Unacceptable.** This study shows that the subject product elicits an anti-feeding effect in stable

flies for up to 28 days on dogs weighing up to 19.01 kg (41.91 lbs) at application rates of 14.50 mg imidacloprid/kg, 71.51 mg permethrin/kg, and 0.66 mg pyriproxyfen/kg (assuming a density of 1.152 g/ml). A >90% reduction in blood feeding on T2 treated dogs was reported for each anti-feeding effect assessment day, regardless of whether geometric or arithmetic means were used. However, because the tested rates exceed the proposed labeled rates, this study **cannot support any** efficacy claims. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg).

This study also supports that the subject product repels stable flies at the tested rates mentioned above for up to 28 days. There was a 100% reduction in probing behavior in stable flies that were exposed to T2 treated dogs regardless of whether geometric or arithmetic means were used. However, because the tested rates exceed the proposed labeled rates, this study **cannot support any** efficacy claims. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg).

This study also supports that the subject product kills fleas at the tested rates mentioned above for up to 12 hours. Following flea introduction to the test animals 2 days prior to test substance administration, there was a >90% reduction in on-animal fleas in dogs treated with T2. Efficacy was not investigated beyond 12 hours, so efficacy claims beyond 12 hours cannot be supported by this study. However, because the tested rates exceed the proposed labeled rates, this study **cannot support any** efficacy claims. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg).

This study **does not** support that the subject product knocks down or kills stable flies at the tested rates mentioned above. While the reported efficacy in both studies did exceed 90% in T2 treated dogs, control mortality was unacceptably high. Control mortality should not exceed 10% at any time point.

49788708. de Vos, C. (2015) A Study to Determine the Effect of Water Immersion and Shampooing on the Efficacy of T2 against Fleas (*Ctenocephalides felis*) on Dogs Final Report. Project Number: CV/15/150, PN1767. Unpublished study prepared by ClinVet International (Pty) Ltd. 106p.

(1) GLP

(2) **Methods:** This study evaluated the efficacy of T2 formulation (Batch number T2MD04) against cat fleas (*Ctenocephalides felis*) when applied topically to dogs. The effect of both water immersion and shampooing on efficacy against fleas was also investigated. T2 formulation contains the same active ingredients as the subject product, but at slightly different concentrations (8.67% imidacloprid, 45.21% permethrin, and 0.42% pyriproxyfen). Thirty-two dogs were divided into 4 groups, each containing 8 dogs (5 males/3 females in each group). Dogs in Group 1 served as the control group and were treated with mineral oil. Dogs in Group 2 were treated with a spot-on application of T2. Dogs in Group 3 were treated with a spot-on application of T2 and immersed in water. Dogs in Group 4 were treated with a spot-on application of T2 and shampooed. Of the dogs in Group 1, 7 ranged in weight from 10.8-24.6 kg and received a 2.5 ml dose of mineral oil, and 1 dog weighed 25.6 kg and received a 4.0 ml dose of mineral oil. Of the dogs in Group 2, 7 ranged in weight from 10.4-21.2 kg and received a 2.5 ml dose of T2, and 1 dog weighed 25.6 kg and received a 4.0 ml dose of T2. Of the dogs in Group 3, 7 ranged in weight from 10.6-20.4 kg and received a 2.5 ml dose of T2, and 1 dog weighed 26.4 kg and received a 4.0 ml dose of T2. All 8 dogs in Group 4 weighed 13.8-22.0 and received a 2.5 ml dose of T2.

The test substance or mineral oil was administered to dogs on day 0. Dogs weighing 9-25 kg received the application in 3 spots. Dogs weighing >25 kg received the application in 4 spots. The doses for each dog in Groups 2-4 have been calculated and are as follows:

Dog's weight (kg)	Amount of T2 applied (ml)	Dose of imidacloprid (mg/kg)*	Dose of permethrin (mg/kg)*	Dose of pyriproxyfen (mg/kg)*
GROUP 2				

17.40	2.5	14.35	74.83	0.70
13.80	2.5	18.09	94.35	0.88
10.40	2.5	24.01	125.20	1.16
18.80	2.5	13.28	69.26	0.64
21.20	2.5	11.78	61.42	0.57
25.60	4.0	15.61	81.38	0.76
18.80	2.5	13.28	69.26	0.64
18.40	2.5	13.57	70.76	0.66
Group 2 Averages				
18.05	--	15.50	80.81	0.75
GROUP 3				
19.00	2.5	13.14	68.53	0.64
26.40	4.0	15.13	78.91	0.73
15.80	2.5	15.80	82.41	0.77
13.00	2.5	19.21	100.16	0.93
10.60	2.5	23.56	122.83	1.14
11.00	2.5	22.70	118.37	1.10
20.40	2.5	12.24	63.83	0.59
13.60	2.5	18.36	95.74	0.89
Group 3 Averages				
16.23	--	17.52	91.35	0.85
GROUP 4				
14.20	2.5	17.58	91.69	0.85
22.00	2.5	11.35	59.18	0.55
19.80	2.5	12.61	65.76	0.61
20.20	2.5	12.36	64.46	0.60
16.20	2.5	15.41	80.37	0.75
15.40	2.5	16.21	84.55	0.79
18.00	2.5	13.87	72.34	0.67
13.80	2.5	18.09	94.35	0.88
Group 4 Averages				
17.45	--	14.69	76.59	0.71

* A density of 1.152 g/ml was assumed

All dogs were acclimatized beginning on day -7. Approximately 100 adult fleas were introduced to the skin of each animal on Days -7, -2, 7, 14, 21, and 28. Live fleas on each animal were combed out and counted 48 hours after test substance/mineral oil administration or flea infestations (Days 2, 9, 16, 23, and 30). Group 1 and 3 dogs were fully immersed in water (including each dog's head) on Days 2, 9, 16, and 23 after flea counts were made on each of those days. Group 1 and 4 dogs were also shampooed on Days 9 and 23, although Group 4 dogs were only rinsed and not fully immersed in water. Dogs were rinsed thoroughly after being shampooed. Geometric means as well as arithmetic means of flea counts were reported, although only arithmetic mean data will be reviewed here. Percent efficacy against fleas was calculated with the following formula:

Percent Efficacy = 100 x $(M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean number of live fleas on dogs in the mineral oil group (Group 1) at a specific time point.

M_t = Geometric or arithmetic mean number of live fleas on dogs in the T2 treatment group (Groups 2, 3, and 4) at a specific time point.

(3) **Results:** Flea counts at the time points tested are summarized below using arithmetic means:

Day	Group 1 Mean (Control)	Group 2 Mean (Treatment)	Percent Efficacy	Group 3 Mean (Treatment)	Percent Efficacy	Group 4 Mean (Treatment)	Percent Efficacy
2	57.8	0.0	**100.0**	0.0	**100.0**	0.0	**100.0**
9	73.0	0.0	**100.0**	0.0	**100.0**	0.0	**100.0**
16	67.0	0.0	**100.0**	0.0	**100.0**	4.3	**93.7**
23	71.5	0.0	**100.0**	0.1	**99.8**	7.1	**90.0**
30	73.4	0.0	**100.0**	1.1	**98.5**	29.5	59.8

Percent efficacy on all flea count days was reported as >90% with the exception of Day 30 for Group 4 dogs (59.8%). The number of live fleas recovered from dogs in Group 1 is sufficient for study to support the subject product. The table above contains percent efficacy figures for each flea count day. Values >90% are bolded.

(4) **Conclusion: Unacceptable.** This study supports that the subject product kills fleas for up to 30 days on dogs weighing up to 18.05 kg (39.79 lbs) at application rates of 15.50 mg imidacloprid/kg, 80.81 mg permethrin/kg, and 0.75 mg pyriproxyfen/kg (assuming a density of 1.152 g/ml). Forty-eight hours after flea introductions to the test animals in Group 2, there was a >90% reduction in on-animal fleas in dogs treated with T2. However, because the tested rates exceed the proposed labeled rates, this study **cannot support any** efficacy. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg).

This study also supports that the subject product kills fleas despite weekly water immersion for up to 30 days on dogs weighing up to 16.23 kg (35.78 lbs) at application rates of 17.52 mg imidacloprid/kg, 91.35 mg permethrin/kg, and 0.85 mg pyriproxyfen/kg (assuming a density of 1.152 g/ml). Forty-eight hours after flea introductions to the test animals in Group 3, there was a >90% reduction in on-animal fleas in dogs treated with T2. However, because the tested rates exceed the proposed labeled rates, this study **cannot support any** efficacy claims. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg).

This study also supports that the subject product kills fleas despite bi-weekly shampooing for up to 23 days on dogs weighing up to 17.45 kg (38.47 lbs) at application rates of 14.69 mg imidacloprid/kg, 76.59 mg permethrin/kg, and 0.71 mg pyriproxyfen/kg (assuming a density of 1.152 g/ml). Forty-eight hours after flea introductions to the test animals in Group 4, there was a >90% reduction in on-animal fleas in dogs treated with T2, with the exception of the final flea introduction on Day 28. Percent efficacy **did not** reach the 90% threshold when fleas were subsequently counted on Day 30 (reported as 59.8%). Moreover, because the tested rates exceed the proposed labeled rates, this study **cannot support any** efficacy claims. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg). Efficacy should also be sustained for a minimum of 4 weeks despite water immersion/shampooing.

49788709. de Vos, C. (2015) Efficacy Study of T2 against the Further Development of Flea (*Ctenocephalides felis*) Eggs Collected from Dogs Infested with Gravid Fleas Final Report. Project Number: CV/15/151, PN1767. Unpublished study prepared by ClinVet International (Pty) Ltd. 105p.

(1) GLP

(2) **Methods:** This study evaluated the efficacy of T2 formulation (Batch number T2MD04) against cat flea (*Ctenocephalides felis*) eggs and development to adulthood when applied topically to dogs. T2 formulation contains the same active ingredients as the subject product, but at slightly different concentrations (8.67% imidacloprid, 45.21% permethrin, and 0.42% pyriproxyfen). Sixteen dogs were divided into two groups, each containing 8 dogs (2 males/6 females in Group 1; 1 male/7 females in Group 2). Dogs in Group 1 served as the control group and were treated with mineral oil, while dogs in Group 2 were treated with a spot-on application of T2. The 8 dogs in Group 2 ranged in weight from 11.0-23.2 kg (average weight of 17.30 kg) and received a 2.5 ml dose of T2. The 8 dogs in Group 1 ranged in weight from 14.0-20.8 kg and received a 2.5 ml dose of mineral oil.

The test substance or mineral oil was administered to dogs on day 0. All dogs weighed 9-25 kg and received the application in 3 spots. The doses for each dog in Group 2 have been calculated and are as follows:

Dog's weight (kg)	Amount of T2 applied (ml)	Dose of imidacloprid (mg/kg)*	Dose of permethrin (mg/kg)*	Dose of pyriproxyfen (mg/kg)*
16.80	2.5	14.86	77.50	0.72
15.60	2.5	16.01	83.46	0.78
18.20	2.5	13.72	71.54	0.66
23.20	2.5	10.76	56.12	0.52
15.40	2.5	16.21	84.55	0.79
18.20	2.5	13.72	71.54	0.66
20.00	2.5	12.49	65.10	0.61
11.00	2.5	22.70	118.37	1.10
Averages				
17.30	2.5	15.06	78.52	0.73

* A density of 1.152 g/ml was assumed

All dogs were acclimatized beginning on day -14. Approximately 100 gravid adult female fleas (collected from infested donor dogs) were introduced to the skin of each animal on Days 1, 28, 56, 70, and 84. Dogs were held overnight in cages designed to collect eggs that had been laid and dropped to the bottom. A target of 50 eggs per animal was collected at each time point. Eggs were collected from Group 1 and 2 dogs 1 day after flea infestations (Days 2, 29, 57, 71, and 85). Eggs were then transferred to petri dishes and held in conditions favorable for flea development for a period of 28 days. Ovicidal assessments (% egg hatch) were conducted 3 days after eggs were collected or 4 days post infestation (Days 5, 32, 60, 74, and 88). The number of emerged adults was counted 28 days after eggs were collected or 29 days post infestation (Days 30, 57, 85, 99, and 113). Live but unemerged pupae on the twenty-eighth day were counted as adults. Geometric means as well as arithmetic means of hatched larvae and emerged adults were reported. Percent efficacy was calculated on each day hatched larvae/emerged adults were counted with the following formula:

Percent Efficacy = 100 x $(M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean of the proportion of hatched larvae/emerged adults in the mineral oil group (Group 1) at a specific time point.

M_t = Geometric or arithmetic mean of the proportion of hatched larvae/emerged adults in the T2 treatment group (Group 2) at a specific time point.

(3) **Results:** Ovicidal effect (% hatched larvae) at the time points tested are summarized below using geometric means:

Flea Infestation Day	Egg Collection Day	Ovicidal Assessment Day	Group 1 Mean (Control)	Group 2 Mean (Treatment)	Percent Efficacy
1	2	5	79.3	0.7	**99.1**
28	29	32	76.3	2.1	**97.2**
56	57	60	73.4	9.5	87.0
70	71	74	88.7	19.1	78.5
84	85	88	84.0	18.5	77.9

Ovicidal effect (% hatched larvae) at the time points tested are summarized below using arithmetic means:

Flea Infestation	Egg	Ovicidal	Group 1 Mean	Group 2 Mean	Percent

Day	Collection Day	Assessment Day	(Control)	(Treatment)	Efficacy
1	2	5	79.8	2.1	**97.4**
28	29	32	76.8	15.0	80.5
56	57	60	74.5	15.6	79.0
70	71	74	88.8	27.0	69.6
84	85	88	84.3	22.0	73.9

Adult emergence inhibition (% emerged adults) at the time points tested are summarized below using geometric means:

Flea Infestation Day	Egg Collection Day	Adult Emergence Assessment Day	Group 1 Mean (Control)	Group 2 Mean (Treatment)	Percent Efficacy
1	2	30	69.4	0.1	**99.8**
28	29	57	61.6	2.1	**96.6**
56	57	85	69.8	9.5	86.4
70	71	99	61.8	8.2	86.8
84	85	113	60.7	12.7	79.1

Adult emergence inhibition (% emerged adults) at the time points tested are summarized below using arithmetic means:

Flea Infestation Day	Egg Collection Day	Adult Emergence Assessment Day	Group 1 Mean (Control)	Group 2 Mean (Treatment)	Percent Efficacy
1	2	30	70.0	0.3	**99.6**
28	29	57	63.5	15.0	76.4
56	57	85	70.8	14.7	79.2
70	71	99	64.0	11.5	82.0
84	85	113	61.3	15.0	75.5

For ovicidal effect, % efficacy was reported as >90% on Days 5 and 32 when using geometric means. These eggs were collected from flea infestations which began on Days 1 and 28, respectively. All days beyond Day 32 produced % efficacy figures below 90%. Using arithmetic means, % efficacy was reported as >90% on Day 5 only. These eggs were collected from flea infestations which began on Day 1. All days beyond Day 5 produced % efficacy figures below 90%.

For adult emergence inhibition, % efficacy was reported as >90% on Days 30 and 57 when using geometric means. These eggs were collected from flea infestations which began on Days 1 and 28, respectively. All days beyond Day 57 produced % efficacy figures below 90%. Using arithmetic means, % efficacy was reported as >90% on Day 30 only. These eggs were collected from flea infestations which began on Day 1. All days beyond Day 30 produced % efficacy figures below 90%.

The tables above contain percent efficacy figures for each day hatched larvae/emerged adults were counted. Values >90% are bolded.

(4) **Conclusion: Unacceptable.** This study does not support any flea IGR claims for the subject product. The Agency prefers the use of arithmetic means for efficacy studies that rely on count data, as is the case here. Geometric means are more appropriate for continuous data that follow a log-normal distribution. Ovicidal effect only surpassed 90% on Day 5. Those eggs were collected from flea infestations which began on Day 1, 1 day after the test substance was administered. As the dosing interval for this product is once per month, it is insufficient to claim flea IGR effects for a duration of 1 day after treatment. Similarly, adult emergence inhibition only surpassed 90% on Day 30. Those eggs were also collected from flea infestations which began on Day 1, 1 day after the test

substance was administered so the same analysis applies.

This study could only support efficacy claims on dogs weighing up to 17.30 kg (38.14 lbs) at application rates of 15.06 mg imidacloprid/kg, 78.52 mg permethrin/kg, and 0.73 mg pyriproxyfen/kg (assuming a density of 1.152 g/ml). Because the tested rates exceed the proposed labeled rates, this study **could not support any** efficacy claims. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg).

49788710. Neethling, W. (2015) A Study to Assess the Efficacy of T2 Formulation to Control Fleas (*Ctenocephalides felis*) in a Dog's Environment Through Assessing Flea Egg Development In Vitro on Carpet Samples Final Report. Project Number: CV/15/152, PN1767. Unpublished study prepared by ClinVet International (Pty) Ltd. 99p.

(1) GLP

(2) **Methods:** This study evaluated the larvicidal efficacy of T2 formulation (Batch number T2MD04) against cat flea (*Ctenocephalides felis*) eggs when applied topically to dogs. The investigators attempted to determine if carpet samples taken from the area where a T2 treated dog sleeps reduce the percentage of adult flea development. T2 formulation contains the same active ingredients as the subject product, but at slightly different concentrations (8.67% imidacloprid, 45.21% permethrin, and 0.42% pyriproxyfen). Sixteen dogs were divided into two groups, each containing 8 dogs (4 males/4 females in Groups 1 and 2). Dogs in Group 1 served as the control group and were treated with mineral oil, while dogs in Group 2 were treated with a spot-on application of T2. The 8 dogs in Group 2 ranged in weight from 13.0-20.8 kg (average weight of 17.20 kg) and received a 2.5 ml dose of T2. Of the dogs in Group 1, 7 ranged in weight from 12.2-20.2 kg and received a 2.5 ml dose of mineral oil, and 1 dog weighed 25.4 kg and received a 4.0 ml dose of mineral oil.

The test substance or mineral oil was administered to dogs on day 0. Dogs weighing 9-25 kg received the application in 3 spots and dogs weighing >25 kg received the application in 4 spots. The doses for each dog in Group 2 have been calculated and are as follows:

Dog's weight (kg)	Amount of T2 applied (ml)	Dose of imidacloprid (mg/kg)*	Dose of permethrin (mg/kg)*	Dose of pyriproxyfen (mg/kg)*
20.80	2.5	12.00	62.62	0.58
17.80	2.5	14.03	73.17	0.68
17.80	2.5	14.03	73.17	0.68
13.00	2.5	19.21	100.19	0.93
13.00	2.5	19.21	100.19	0.93
20.00	2.5	12.49	65.13	0.61
14.80	2.5	16.87	88.01	0.82
20.40	2.5	12.24	63.85	0.59
Averages				
17.20	2.5	15.01	78.29	0.73

* A density of 1.152 g/ml was assumed

Flea eggs used in this study were collected from untreated donor dogs. Dogs were treated with either mineral oil or T2 on Day 0. Each dog's sleeping bench was entirely covered with a piece of carpet measuring 96 cm x 67 cm beginning on Day 0. On Days 7, 28, 56, 77, and 84, 3 circular samples measuring 6.5 cm in diameter were cut from each piece of carpet and placed in petri dishes with the same diameter. Sleeping benches were covered with new carpet pieces on days carpet samples were taken (except Day 84). The samples were taken from areas of the carpet where the dog spent the most time, as indicated by the amount of deposited hair. On the same day, each circular sample was seeded with approximately 100 flea eggs and flea growth medium to facilitate larval development. Petri dishes containing seeded carpet samples were kept in conditions favorable for larval development and assessed for

number of emerged adults 28 days later (on Days 35, 56, 84, 105, and 112). Live but unemerged pupae on the twenty-eighth day were counted as adults.

Percent efficacy was calculated on each day emerged adults were counted with the following formula:

Percent Efficacy = 100 x $(M_c - M_t)/M_c$, where:

M_c = Arithmetic mean number of the proportion of emerged adults in the mineral oil group (Group 1) at a specific time point.

M_t = Arithmetic mean number of the proportion of emerged adults in the T2 treatment group (Group 2) at a specific time point.

(3) **Results:** Adult emergence inhibition (% emerged adults) at the time points tested are summarized below using arithmetic means:

Carpet Seeding Day	# of Days Carpet Exposed to Dog	Adult Emergence Assessment Day	Group 1 Mean Number of Emerged Adults (Control)	Group 2 Mean Number of Emerged Adults (Treatment)	Percent Efficacy
7	7	35	24.6	0.3	**99.0**
28	21	56	10.1	0.0	**100.0**
56	28	84	23.7	0.0	**100.0**
77	21	105	45.5	2.4	**94.8**
84	7	112	72.8	14.7	79.8

Percent efficacy on all days adult emergence inhibition was assessed was reported as >90%, with the exception of Day 112 (seeded on Day 84). The tables above contain percent efficacy figures for each day emerged adults were counted. Values >90% are bolded.

(4) **Conclusion: Unacceptable.** This study does not support any flea IGR claims. Out of the 100 eggs added to each control carpet sample, only 10.1-45.5% adult emergence was observed. The mean number of emerged adults rose to 72.8 in the samples seeded on Day 84, but percent efficacy was only 79.8%. This is inadequate to support any efficacy claims. Percent adult emergence in the control group samples should be consistently above 70%. Moreover, the study investigators' sampling bias of taking 3 carpet samples from the most frequented areas on the sleeping bench represents the most favorable chance of efficacy being observed. A more realistic sampling method in which the samples were taken from three equally spaced locations on the sleeping bench would have been more appropriate. The experimental design is not sufficient to support the desired efficacy claim of "prevents the further development of immature flea life stages in the environment, namely flea eggs, larvae, and pupae for 12 weeks."

An additional problem is that this study used dogs weighing an average of 17.20 kg (37.92 lbs) with corresponding application rates of 15.01 mg imidacloprid/kg, 78.29 mg permethrin/kg, and 0.73 mg pyriproxyfen/kg (assuming a density of 1.152 g/ml). Because the tested rates exceed the proposed labeled rates, this study **could not support any** efficacy claims. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg).

49788711. Neethling, W. (2015) A Randomised, Negative Controlled Study Assessing the Efficacy of Formulation T2 in the Prevention of Flea (*Ctenocephalides felis*) Infestations on Dogs in a Simulated Home Environment Final Report. Project Number: CV/15/153, PN1767. Study prepared by ClinVet International (Pty) Ltd. 114p.

(1) GLP

(2) **Methods:** This study evaluated the efficacy of T2 formulation (Batch number T2MD01 or T2MD04 – not

specified) against adult cat fleas (*Ctenocephalides felis*) when applied topically to dogs. The investigators attempted to determine if T2 treated dogs experienced reduced flea infestations after repeated introductions of flea pupae to the dog's kennel. T2 formulation contains the same active ingredients as the subject product, but at slightly different concentrations (8.67/8.7% imidacloprid, 45.17/45.21% permethrin, and 0.42% pyriproxyfen). Sixteen dogs were divided into two groups, each containing 8 dogs (4 males/4 females in Groups 1 and 2). Since it was not specified whether T2MD01 or T2MD04 was used, this review will consider the higher concentration of each active ingredient for efficacy determinations. This represents the most conservative approach. Of the dogs in Group 2, 7 ranged in weight from 14.40-24.60 kg and received a 2.5 ml dose of T2, and 1 dog weighed 25.40 kg and received a 4.0 ml dose of T2. The 8 dogs in Group 1 ranged in weight from 13.60-24.40 kg and received a 2.5 ml dose of mineral oil.

The test substance or mineral oil was administered to dogs on day 0 and again on day 30. Dogs weighing 9-25 kg received the application in 3 spots and dogs weighing >25 kg received the application in 4 spots. The doses for each dog in Group 2 have been calculated and are as follows:

Dog's weight (kg)	Amount of T2 applied (ml)	Dose of imidacloprid (mg/kg)*	Dose of permethrin (mg/kg)*	Dose of pyriproxyfen (mg/kg)*
14.60	2.5	17.16	89.18	0.83
16.60	2.5	15.09	78.44	0.73
14.40	2.5	17.40	90.42	0.84
24.60	2.5	10.19	52.93	0.49
17.80	2.5	14.08	73.15	0.68
25.40	4.0	15.78	82.02	0.76
21.20	2.5	11.82	61.42	0.57
15.80	2.5	15.86	82.41	0.77
Averages				
18.80	--	14.67	76.25	0.71

* A density of 1.152 g/ml was assumed

Each dog's cage was provided with a sleeping kennel, the bottom of which was covered with carpet. Approximately 100 flea pupae were introduced to the sleeping kennel on Days -14, -7, 0, 14, 28, and 42 via an apparatus mounted to the top of the kennel. The apparatus was designed in such a way that newly emerged adult fleas would jump over a barrier and fall down to the carpeted bottom below where each dog slept, thereby infesting the dog. Therefore, pupae introduced to the apparatus were not directly exposed to the T2/mineral oil-treated dog or carpet. Live adult fleas on each animal were combed out and counted on Days -5, 2, 7, 14, 21, 28, 35, 42, 49, and 56. Any live fleas that were recovered at these time points were reintroduced to the same animal on the same day. On Day 63, live adult fleas were combed out and counted but not reintroduced to the animal. Geometric means as well as arithmetic means of flea counts were reported, although only arithmetic mean data will be reviewed here. Percent efficacy against fleas was calculated with the following formula:

Percent Efficacy = $100 \times (M_c - M_t)/M_c$, where:

M_c = Geometric or arithmetic mean number of live and moribund fleas on dogs in the mineral oil group (Group 1) at a specific time point.

M_t = Geometric or arithmetic mean number of live and moribund fleas on dogs in the T2 treatment group (Group 2) at a specific time point.

(3) **Results:** On-animal efficacy at the time points tested are summarized below using arithmetic means:

Day Adult Fleas Counted	Group 1 Mean # of Living + Moribund Adult Fleas (Control)	Group 2 Mean # of Living + Moribund Adult Fleas (Treatment)	Percent Efficacy
2	85.4	0.0	**100.0**

7	80.6	0.1	**99.8**
14	78.1	0.3	**99.7**
21	48.9	0.1	**99.7**
28	54.0	0.5	**99.1**
35	39.0	0.0	**100.0**
42	56.3	0.0	**100.0**
49	53.4	0.0	**100.0**
56	68.5	0.0	**100.0**
63	45.9	0.0	**100.0**

Percent efficacy on all days on-animal adult fleas were counted was reported as >90%. The table above contains percent efficacy figures for each day live/moribund on-animal adult fleas were counted. Values >90% are bolded.

(4) **Conclusion: Unacceptable.** This study supports that the subject product kills adult fleas and prevents flea reinfestations for up to 28 days on dogs weighing up to 18.80 kg (41.45 lbs) at application rates of 14.67 mg imidacloprid/kg, 76.25 mg permethrin/kg, and 0.71 mg pyriproxyfen/kg (assuming a density of 1.152 g/ml). There was a >90% reduction in on-animal fleas in dogs treated with T2 following introductions of pupae to each dog's sleeping kennel 28 days after T2/mineral oil was applied. A second dose was administered on Day 30, so efficacy claims cannot extend to the final adult flea count day (Day 63). Also, because the tested rates exceed the proposed labeled rates, this study **cannot support any** efficacy claims. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg). This study does not support flea IGR claims as efficacy against juvenile development was not investigated.

49788712. Meyer, J. (2015) Review of Scientific Literature Associated with Efficacy of Imidacloprid and Permethrin against Chewing Lice, *Trichodectes canis*, Infestations on Dogs. Unpublished study prepared by Triveritas Ltd. 7p.

(1) Literature Review. non-GLP.

(2) **Supplemental.** This MRID contains a literature review of various imidacloprid, permethrin, and pyriproxyfen products used to control various ectoparasites on dogs. It does not present any data to support the subject product and can only be considered supplemental in nature. Data should be presented to support desired efficacy claims against chewing lice.

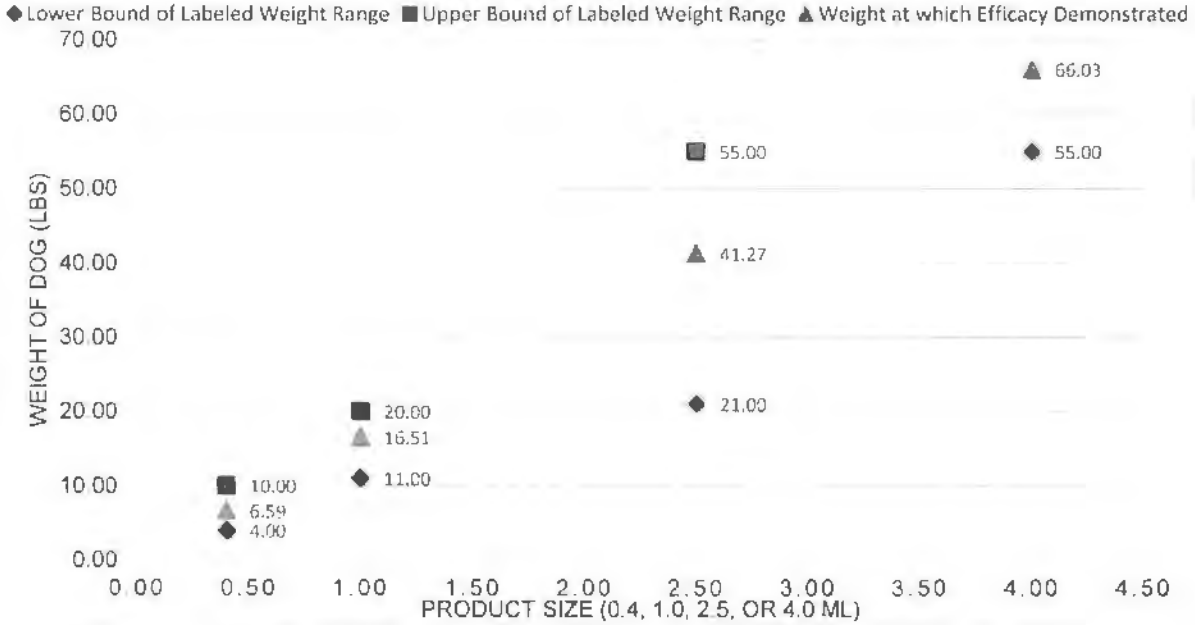
IV. EXECUTIVE DATA SUMMARY:

(A) The data do not support any efficacy claims against fleas, ticks, mosquitoes, biting flies, or lice. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg). However, the doses used in all studies submitted to support this product are notably higher than the dose that would be received by dogs at the upper end of each weight range. The average weight at which efficacy is demonstrated should be greater than or equal to the upper bound of each labeled weight range. Figure 1 below illustrates this discrepancy.

Quick kill/fast knockdown type claims, as well as waterproof/effective after shampooing/rainproof claims against any public health pest are not supported by these data for the same reason stated above.

Flea IGR claims are not supported. This includes egg/ovicidal, larvae/larvicidal, and pupae claims. All claims that the subject product is efficacious against fleas in the home environment are similarly not supported by these data.

FIGURE 1: WEIGHT AT WHICH EFFICACIOUS DOSE DEMONSTRATED



V. LABEL RECOMMENDATIONS:

(1) The following changes in the Directions for Use are suggested:

N/A

(2) The following marketing claims are acceptable:

- T2.200 contains imidacloprid, permethrin, and the insect growth regulator pyriproxyfen

(3) The following marketing claims are unacceptable:

- All flea, tick, mosquito, biting fly, and lice efficacy claims are unacceptable. This includes waterproof/shampoo-proof/rainproof/water immersion claims and all IGR claims or claims against various life stages of the aforementioned pests.

- While some but not all of the data submitted to support efficacy claims for this proposed product could be adequate, the doses used throughout are not. Studies investigating the efficacy of spot-on products should determine the appropriate dose of test material based on a dose titration approach, such that all animals receive the lowest possible dose according to proposed weight ranges (in this case 8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg). It is not sufficient to apply one of the four proposed doses for each animal based on which of the four corresponding weight ranges it falls into, as was seen here. Doing so prevents study investigators and Agency reviewers from being able to determine if the product is efficacious on dogs at the very upper end of each weight range (see Figure 1 above). It is essential that the lowest labeled rate/dose is used in studies which are submitted or cited to support efficacy claims.

(4) The following MRIDs should be removed from the data matrix, as they are classified as "unacceptable" to support the product:

49788701
49788702
49788703
49788704
49788705
49788706
49788707
49788708
49788709
49788710
49788711

(5) Note to reviewer/PM:

MRID 49788706 shows that the subject product kills and prevents blood feeding by *Ae. aegypti* mosquitoes for up to 29 days on dogs weighing up to 18.48 kg (40.74 lbs) at application rates of 15.84 mg imidacloprid/kg, 82.25 mg permethrin/kg, and 0.76 mg pyriproxyfen/kg. However, this study **does not** support general mosquito claims. Given the proposed upper bounds of each weight range (10, 20, and 55 lbs), sufficient efficacy should be demonstrated at the existing proposed lowest labeled rates (8.94 mg imidacloprid/kg, 44.70 mg permethrin/kg, and 0.45 mg pyriproxyfen/kg). In addition, representative species from the genera *Culex*, *Aedes*, and *Anopheles* should be tested for a general mosquito claim. The Agency's rationale for this is that these three genera encompass most of the important disease vectors in the United States. In addition, the average consumer is unable to distinguish an *Aedes* species, let alone *Ae. aegypti* from other mosquitoes.

For a biting flies claim to be supported, efficacy should be demonstrated against biting midges (*Culicoides* spp.), stable flies (*Stomoxys calcitrans*), and black flies (one of either a *Simulium* or *Prosimulium* sp.). Only stable fly data were submitted to support this product.

An upper bound should be given for the largest weight range. Currently, the proposed label suggests a 4.0 ml dose for dogs weighing greater than 55 lbs. The dose used in efficacy studies to support this product should be equal to or less than the dose received by a dog at the very upper bound of each weight range.

CAP IM Supply, Inc.
303 Perimeter Center North, Suite 300
Atlanta, GA 30346

July 22, 2016

submit data
Possibility to
extend based
on what-
type of
review is
required

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)

Re: T2.200 for Dogs (EPA File Symbol 91384-G)

Dear Beth,

In preparation for our potential discussion on Tuesday (7/26), I wanted to provide a summary of information on our packaging for T2.200 (91384-G), including confirmatory information gathered this week with our supplier and testing lab.

Application for new registration was delivered to EPA on December 7, 2015. This filing was made with platines of HDPE pipettes designed without an outer CR blister.

- These pipettes were successfully tested for CR and senior-friendly properties in the data (MRIDs) submitted with the application.
- These pipettes were also reviewed and approved in filings under our CAP Supply, Inc. company name for 91019-1, 91019-2. This product package has not yet been commercialized in the US, but is subject to 6(a)(2) reporting.
- The HDPE pipettes passed testing under accelerated storage stability conditions for both chemical stability and corrosion stability.
- We have subsequently reviewed retained lab samples and are comfortable that we can launch the T2.200 product in this package.

Only in *stress testing* this HDPE package in a pure solvent mixture (not the T2.200 for Dogs formulation), we have noticed some corrosion in the packaging. Although this was an extreme test, our goal remains to find a way to switch to a more desired package for T2.200 for Dogs in the most expeditious manner possible within the bounds of common sense and the Agency's PRIA policies.

Subsequent to our filing in December, 2015, we received positive results from stress testing an alternate packaging laminate with Cyclic Olefin Copolymer (COC) as the inner barrier. We have been working diligently to complete testing on this new package and feel it is a better consumer option for the T2.200 formulation.

- We have tested the COC laminate in a proven design that has an outer CR blister, because we were not confident that the COC laminate (film)

would support CR properties, without an outer CR blister. This additional testing was performed in Q1, 2016 and the data were submitted in our June 13, 2016 submission.

- This design includes an outer CR blister in the same configuration and materials used in several currently commercialized products including 91019-1, 91019-2. Quarterly 6(1)(2) reporting is being followed for these products.
- This package has passed accelerated stability with the T2.200 formulation for both chemical properties and corrosion.

We appreciate the EPAs assistance in determining the appropriate timing for review and approval of the new packaging and transition for T2.200 for Dogs at the earliest possible point.

Thank you,

John Tatum – COO
CAP IM Supply, Inc.

Explanatory Notes Regarding 3-Page Report of Klocke Verpackungs-Service GmbH Stability Testing Product Number: 68223, Batch Number: S3315N 50/50 Mixture of N-Methylpyrrolidone and DMSO Conducted Between April 23, 2015 and October 23, 2015

German to English Translations Not Shown within Tables of the Report:

German	English
Keine	None
I.O	OK
N I.O	Not OK
Leichte delamination	Slight delamination

German to English Translation of Final Assessment on Page 3 of the Report:

04.05.2015	bottom foil:	Inner layer HDPE can be easily separated; unopened pipette is unobtrusive.
	lid foil:	foil is contaminated on the outside by the filling; delamination
13.05.2015	bottom foil:	Inner layer HDPE can be easily separated; unopened pipette is unobtrusive.
	lid foil:	foil is contaminated on the outside by the filling; delamination
22.05.2015	bottom foil:	Inner layer HDPE can be easily separated; unopened pipette is unobtrusive.
	lid foil:	foil is contaminated on the outside by the filling; delamination
23.07.2015	bottom foil:	Inner layer HDPE can be easily separated; unopened pipette is unobtrusive.
	lid foil:	foil is contaminated on the outside by the filling; delamination
23.10.2015	Result:	
	bottom foil:	Inner layer HDPE can be easily separated; unopened pipette is unobtrusive.
	lid foil:	foil is contaminated on the outside by the filling; delamination
	Filling:	visual OK
	Weighing testing:	increase of weight

Explanation of Weight Testing:

The individual pipettes were weighed.

KLOCKE

VERPACKUNGS-SERVICE GmbH Weingarten

Nr.:	FB-131
Version:	05
Seite:	1 von 3

Formblatt: Stabilitätsprüfung

form: stability testing

Kunde: *client*	KLOCKE (Stabi-Test in CRP-Folie für neue Lösungsmittelkombination)		**Produkt-Nr.:** *Product no*	68223	**Chargen-Nr.:** *Batch no* S3315N
Produkt: *product*	N-Methylpyrrolidone + DMSO (3,00ml)	N-Methylpyrrolidone 500 ml DMSO: 500ml	**Bodenfolie:** *Bottom foil*	Mat.Nr.86041 CPAw/CPP/COC/HDPE 50/100/380/50µ -170mm WE: 1410280005 Kd.anl 34650006 Amcor	
Projekt-Nr.: *Project no*	**PA-Nr.:** *Order no* 5077616		**Deckfolie:** *Lidding foil*	Mat.Nr.85342 PETw/OPA/ALU/HDPE 23/25/9/50µ - 170mm WE:1407290006 Kd.anl. 34646292 Amcor	
Lagerbedingungen: *Storage conditions*	Raumtemperatur *room temperature*	X Klimaschrank 38°C / 90% rel. Feuchte *climatic chamber 38 °C / 90 % rH*			

Datum: *date*	23.04.15	24.04.15	27.04.15	04.05.15	13.05.15	22.05.15	23.07.15	23.10.15
Prüfintervall: *Testing interval*	Tag 0 *Day 0*	Tag 1 *Day 1*	Tag 4 *Day 4*	Tag 11 *Day 11*	Tag 20 *Day 20*	*1 Mon.*	*3 Mon.*	*6 Mon.*
Bulkveränderung *Bulk solution changes*	Keine	Keine	Keine	Keine	Keine	Keine	Keine	Keine
Folien *foils*	I.O	I.O	I.O	N I.O	N I.O	N I.O	N I.O	N I.O
Delamination *delamination*	Keine	Keine	Keine	Leichte delamination BoFo,DeFo	Leichte delamination BoFo,DeFo	Leichte delamination BoFo,DeFo	BoFo, DeFo	BoFo, DeFo
→ Deckfolie *Lidding foil*	I.O	I.O	I.O	N I.O	N I.O	N I.O	N I.O	N I.O
→ Bodenfolie *Bottom foil*	I.O	I.O	I.O	N I.O	N I.O	N I.O	N I.O	N I.O
Verfärbung der Folie *Discoloration of foil*	Keine	Keine	Keine	Keine	Keine	Keine	Keine	Keine
Fleckenbildung Innenseite der Folie *Stain formation foil inside*	Keine	Keine	Keine	Keine	Keine	Keine	Keine	Keine
Dichtigkeit *tightness*	I.O	I.O	I.O	N I.O	N I.O	N I.O	N I.O	N I.O
Rückschrumpfverhalten *Back-shrinking behavior*	Keine	Keine	Keine	Keine	Keine	Keine	Keine	Keine
Deformation *deformation*	Keine	Keine	Keine	Keine	Keine	Keine	Keine	Keine
Funktionstest *Function test*								
Abbrechverhalten der Öffnungsnase *functionality of the break off part*	-	-	-	-	-	-	-	-
Aufreißverhalten *Break open functionality*	-	-	-	-	-	-	-	-
Peelverhalten *Peel functionality*	-	-	-	-	-	-	-	-
Durchdrückverhalten *Pushing functionality*	-	-	-	-	-	-	-	-

geprüft:	08.03.13	von:	Freigegeben:	08.03.13	von:
	Datum	Dr. T. Kirchner		Datum	C. Ulrich

KLOCKE

VERPACKUNGS-SERVICE GmbH Weingarten

Nr.:	FB-131
Version:	05
Seite:	2 von 3

Formblatt: Stabilitätsprüfung

form: stability testing

Kunde: *client*	KLOCKE (Stabi-Test in CRP-Folie für neue Lösungsmittelkombination)		**Produkt-Nr.:** *Product no*	68223	**Chargen-Nr.:** *Batch no* S3315N
Produkt: *product*	N-Methylpyrrolidone + DMSO (3,00ml)	N-Methylpyrrolidone 500 ml DMSO: 500ml	**Bodenfolie:** *Bottom foil*	Mat.Nr.86041 CPAw/CPP/COC/HDPE 50/100/380/50µ -170mm WE: 1410280005 Kd.anl 34650006 Amcor	
Projekt-Nr.: *Project no*		**PA-Nr.:** *Order no* 5077616	**Deckfolie:** *Lidding foil*	Mat.Nr.85342 PETw/OPA/ALU/HDPE 23/25/9/50µ - 170mm WE:1407290006 Kd.anl. 34646292 Amcor	
Lagerbedingungen: *Storage conditions*	Raumtemperatur *room temperature*	X Klimaschrank 38°C / 90% rel. Feuchte *climatic chamber 38 °C / 90 % rH*			

Gewichtsprüfung

Weight testing

Datum *date*	23.04.15	24.04.15	27.04.15	04.05.15	13.05.15	22.05.15	23.07.15	23.10.15	
Prüfinterval *Testing interval* →	Tag 0 *Day 0*	Tag 1 *Day 1*	Tag 4 *Day 4*	Tag 11 *Day 11*	Tag 20 *Day 20*	*1 Mon.*	*3 Mon.*	*6 Mon.*	Abweichung *deviation*
Prüfling 21 *Test item*	5,364	5,366	5,368	5,382	5,402	5,418	5,492	5,568	0,204
Prüfling 22	5,105	5,110	5,112	5,124	5,142	5,158	5,229	5,338	0,233
Prüfling 23	5,186	5,188	5,190	5,203	5,223	5,240	5,308	5,387	0,201
Prüfling 24	5,299	5,302	5,304	5,317	5,334	5,355	5,433	5,534	0,235
Prüfling 25	4,825	4,828	4,830	4,843	4,862	4,873	4,948	5,030	0,205
Prüfling 26	5,390	5,393	5,395	5,410	5,426	5,445	5,523	5,624	0,234
Prüfling 27	5,305	5,309	5,311	5,322	5,341	5,359	5,442	5,560	0,255
Prüfling 28	5,476	5,480	5,482	5,494	5,518	5,530	5,603	5,705	0,229
Prüfling 29	5,015	5,017	5,019	5,033	5,057	5,067	5,141	5,205	0,190
Prüfling 30	5,377	5,380	5,382	5,398	5,416	5,434	5,502	5,574	0,197
Prüfling 31	5,055	5,058	5,060	5,076	5,096	5,114	5,177	5,257	0,202
Prüfling 32	5,340	5,343	5,345	5,361	5,380	5,398	5,477	5,562	0,222
Prüfling 33	5,169	5,174	5,175	5,188	5,204	5,221	5,296	5,373	0,204
Prüfling 34	5,039	5,041	5,042	5,059	5,075	5,091	5,169	5,247	0,208
Prüfling 35	5,607	5,609	5,611	5,627	5,642	5,657	5,732	5,880	0,273
Prüfling 36	5,193	5,197	5,199	5,213	5,228	5,244	5,316	5,408	0,215
Prüfling 37	5,406	5,411	5,412	5,428	5,444	5,462	5,525	5,627	0,221
Prüfling 38	5,056	5,059	5,061	5,077	5,095	5,112	5,200	5,298	0,242
Prüfling 39	4,812	4,814	4,816	4,835	4,854	4,872	4,938	5,024	0,212
Prüfling 40	5,022	5,025	5,027	5,041	5,063	5,078	5,148	5,220	0,198
Mittelwert *mean*	5,202	5,205	5,207	5,222	5,240	5,256	5,330	5,421	

KLOCKE

VERPACKUNGS-SERVICE GmbH Weingarten

Nr.:	FB-131
Version:	05
Seite:	3 von 3

Formblatt: Stabilitätsprüfung

form: stability testing

Kunde: *client*	KLOCKE (Stabi-Test in CRP-Folie für neue Lösungsmittelkombination)		**Produkt-Nr.:** *Product no*	68223	**Chargen-Nr.:** *Batch no* S3315N
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Projekt-Nr.: *Project no*		**PA-Nr.:** *Order no* 5077616	**Deckfolie:** *Lidding foil*	Mat.Nr.85342 PETw/OPA/ALU/HDPE 23/25/9/50µ - 170mm WE:1407290006 Kd.anl. 34646292 Amcor	
Lagerbedingungen: *Storage conditions*	Raumtemperatur *room temperature*	X Klimaschrank 38°C / 90% rel. Feuchte *climatic chamber 38 °C / 90 % rH*			

Klima

Abschlussbewertung:
Final assessment
Tara 2,091gr

04.05.2015 BoFo: Innen liegende Schicht HDPE lässt sich leicht lösen.
Im ungeöffneten Zustand ist die Pipette unauffällig
DeFo: Folie ist außen durch das Füllgut kontaminiert. Delamination.

13.05.2015 BoFo: Innen liegende Schicht HDPE lässt sich leicht lösen.
Im ungeöffneten Zustand ist die Pipette unauffällig
DeFo: Folie ist außen durch das Füllgut kontaminiert. Delamination.

22.05.2015 BoFo: Innen liegende Schicht HDPE lässt sich leicht lösen.
Im ungeöffneten Zustand ist die Pipette unauffällig
DeFo: Folie ist außen durch das Füllgut kontaminiert. Delamination.

23.07.2015 BoFo: Innen liegende Schicht HDPE lässt sich leicht lösen.
Im ungeöffneten Zustand ist die Pipette unauffällig
DeFo: Folie ist außen durch das Füllgut kontaminiert. Delamination.

23.10.2015 Ergebnis:

BoFo: Innen liegende Schicht HDPE lässt sich leicht lösen.
Im ungeöffneten Zustand ist die Pipette unauffällig

DeFo: Folie ist außen durch das Füllgut kontaminiert. Delamination.

Füllgut: Optisch I.O
Gewichtsänderung: Zunahme beim Gewicht

Datum *date* / Unterschrift Leitung Sonderverpackung *signature head of special packaging*

Fertich, Elizabeth

From:	Richard L. Conn <richard@connsmith.com>
Sent:	Friday, July 15, 2016 3:15 PM
To:	Fertich, Elizabeth
Cc:	John Tatum; IVB1; Fry, Meridith; David Petrick
Subject:	Re: Additional data submitted for pending EPA File Symbol 91384-G
Follow Up Flag:	Follow up
Flag Status:	Flagged

Hi Beth,
CAP IM Supply sincerely appreciates the discussion and the time you and Meridith took in our 2 PM conference call July 12.

This is the email we promised to send outlining the situation and timing that CAP IM Supply encountered with its packaging for its pending product, T2.200 for Dogs (EPA File Symbol 91384-G). Our goal is to find a way to switch to the more desired package for this product in the most expeditious manner possible within the bounds of common sense and the Agency's PRIA policies, hopefully using the discretion available to you when situations arise that call for creative solutions upon which both the Agency and the registrant can agree.

First of all it is important to know that CAP IM Supply did not decide on a new packaging option until after the application for new registration was delivered to EPA on December 7, 2015. CAP IM Supply quickly pursued steps to arrange for using different packaging (that was known to be acceptable in many similar products already marketed) including accelerated storage stability testing and clarification of what additional Child Resistant Packaging (CRP) data would be needed to satisfy EPA on T2.200 for Dogs if CAP IM Supply switched to different packaging.

The owner of the CRP data for the packaging of T2.200 for Dogs is Klocke Verpackungs - Service GmbH, whose US Agent at EPA is Ann Tillman of Pyxis Regulatory Consulting, Inc. Sometime in early January this year Ann spoke with Maggie Rudick at EPA about the question of what additional CRP testing EPA would require to bridge previously reviewed MRID data on this package to the requirements for T2.200 for Dogs. These requirements include the addition of a slightly smaller fill size (0.4ml) and the addition of packaging in strips of 2 applicators. On January 12, 2016, Ann sent Klocke inputs from those discussions she had with Maggie.

Namely, Maggie commented to Ann that the smallest and largest fill volumes for T2.200 for Dogs should be tested with children only in strips of 2 applicators and then the existing MRID data for strips of 3 can be used to bridge to other fill volumes. Klocke agreed to test 0.4 mL and 4.0 mL consistent with the largest and smallest fill volumes needed for T2.200 for Dogs. All the other Klocke CRP data (strips of 3 applicators) were existing and cited in the data matrix submitted June 13, 2016 and in the letter of authorization from Klocke that is dated May 30, 2016 that we submitted in the June 13 submission package.

Klocke contracted with National Child Resistant Testing, Inc. in Lincoln, NE for the 0.4 mL and 4.0 mL testing and the testing was conducted between January 21 and February 15, 2016, with a final report signed by the author February 23, 2016. We submitted the new CRP data along with the accelerated storage test results June 13 soon after obtaining the needed Klocke letter of authorization and soon after we obtained new PDF copies of the CRP study reports that repaired a problem with Ann Tillman's signature in the original version we had received from Klocke.

It is important to note that 6 of the 8 MRIDs we have cited for CRP data were previously reviewed by EPA for

other actions, and thus only two CRP MRIDs are newly submitted and have not been reviewed by EPA to date. CAP IM Supply will be providing to you the CRP certification for this type of packaging as required by 40 CFR 157.34 by next Tuesday, July 19.

CAP IM Supply believes that our situation is unique, rarely encountered, and that some kind of reasonable solution is called for to allow for a win-win outcome. Perhaps our offer in the following paragraph would be helpful.

Since we realize the Agency would need to use some time to review the CRP data in two new MRIDs we submitted June 13, 2016 on top of having reviewed the original CRP data we had cited in our initial December 7, 2015 submission, CAP IM Supply is hereby committing to help keep the playing field level by offering to pay an additional PRIA fee and accepting the time frame associated with PRIA code R340 (4 months) for review of the additional CRP data we have submitted to support our preferred packaging. The 4-month plus 21 days time frame calculated from the June 13 submission date of the new MRIDs would put the PRIA date for this packaging acceptance at November 3, 2016, which CAP IM Supply would find acceptable. That date is only 36 days beyond the September 28, 2016 PRIA date of the current submission. Using this approach makes logical sense compared to the alternative of CAP IM Supply initially launching this product in CRP packaging that it considers to be less desirable, followed by seeking a CRP packaging amendment under R340 that would take until roughly mid-February 2017 for EPA to finish the regulatory process.

We look forward to your consideration of our proposal as described above for EPA File Symbol 91384-G.

Best regards,
Richard

→ calculate from day of decision on acceptability

On 7/7/2016 1:32 PM, Fertich, Elizabeth wrote:

> John,
> I received the data package submitted on 6/13/16 requesting review of new child-resistant packaging for pending EPA File Symbol 91384-G. Because we are so far along in the review process, we cannot review this data as part of this application. The request for a new type of packaging can be submitted after the registration is granted. This will be a PRIA submission, as review of data will be required. As several reviews are still pending at this time, this is not an indication that you are guaranteed that the registration will be granted. Please contact myself or Meridith Fry if you have any questions.
> Kind regards,
> Beth
>
> Elizabeth Fertich
> US Environmental Protection Agency
> Office of Pesticide Programs
> Registration Division (7505P)
> Invertebrate and Vertebrate Branch 1 (IVB1)
> fertich.elizabeth@epa.gov
> 703-347-8560

Concurrent submission of R340
6/13
21 days
↓
Now due date for original submission

--
Richard L. Conn, President, Conn & Smith, Inc.
6713 Catskill Rd, Lorton VA 22079-1113, USA
Phone: (703) 339-4199
http://www.connsmith.com

Do you have other products using this package?

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS REGISTRATION DIVISION (7505P)

FEE

DOCUMENT CONTAINS CONFIDENTIAL INFORMATION

DPBAR CODE NO.: 431150/431027 **EPA File Symbol NO.: 91384-G** **DECISION NO.: 511951**
PC Code: 109701,129032,129099 **ACTION CODE: R315**
FOOD Use: No

DATE OUT: June 20, 2016

SUBJECT: End Use Product Chemistry Review
Product Name: T2.200For Dogs

FROM: Hari Mukhoty, DVM, PhD.
Product Chemistry Team
CITAB / Registration Division (7505P)

TO: Elizabeth Fertich, RMR / Jennifer Urbanski, RM 04
Invertebrate & vertebrate Branch 1 / Registration Division (7505P)

Company Name: CAP IM Supply, Inc.

INTRODUCTION:

The registrant has submitted a basic CSF (Dated 12/23/2015) and has also proposed a product specific label for registration of the aforesaid product under EPA File Symbol: 91384-G. Product chemistry data have been submitted under MRIDs: 497997-01, 497887-13 and -14.

The aforesaid product was manufactured by the Klocke Verpackungs-Service GmbH, Germany.

CITAB has been requested to evaluate the product chemistry data required for registration of the aforesaid product.

SUMMARY OF FINDINGS:

1. Name of Active Ingredient(s): Imidacloprid (8.80%), Permethrin (44.00%) and Pyriproxyfen (0.44%)..

2. Has the registrant claimed substantial similarity to registered product?

   [ ] Yes [X] No [ ] NA If yes: EPA Reg. No.

3. The source materials of the active ingredients are registered with the Agency [Yes].

4. The CSF have been screened by inert group and they found that inerts are approved for non-food use.

DPBAR CODE NO.: 431150/431027 EPA File Symbol NO.: 91384-G DECISION NO.: 511951
PC Code: 109701,129032,129099 ACTION CODE: R315
FOOD Use: No

5. Confidential Statement of Formula(s):

[X] Basic - Dated: 12/23/2015 Re-submitted: NA
[ ] Alternate - Dated: Re-submitted: NA

Alternate CSF(s) complies with 40CFR §152.43: [ ] Yes [ ] No NA [X]

6. Product label

a. Ingredient statement: Nominal concentrations of AI listed on CSF(s) concur with product label (PR Notice 91-2).

[Yes]

Is the sub statement in compliance with PR Notice 97-6?

[X] Yes [ ] No - Uses the term "Other Ingredients"

, if not, explain below:

Metallic equivalent: [ ] Yes [X] NA
Soluble arsenic: [ ] Yes [X] NA
Isomeric ratios: [ ] Yes [X] NA
Acid equivalent: [ ] Yes [X] NA

b. Health related sub statements:

Petroleum distillate at > 10%: [ ] Yes [ ] No [X] NA
Methanol at > 4%: [ ] Yes [ ] No [X] NA
Sodium Nitrate / Sodium Nitrite [ ] Yes [ ] No [X] NA

c. Physical chemical hazard statement: Product label requires a statement per 40 CFR §156.78 for: flammability, explosive potential or electric insulator breakdown?

[ ] Yes [X] No

Total Release Fogger PR Notice 98-6 (40 CFR 156.78 d): [ ] Yes [X] No [ ] NA

d. Label requires an additional Storage and Disposal statement: [ ] Yes [X] No

Final decision of overall label acceptance will be made by the PM.

7. Group A: Product Chemistry Data

CITAB's determination of the acceptability of the data for the proposed product is listed in the tables below.

Guideline No.	Study Title		Data submitted		CITAB's Assessment of Data	MRID Nos.
			Yes	No		
830.1550	Product Identity & Composition		X		A	497997-01
830.1600	Description of materials used to produce the product		X	"	A	"
830.1650	Description of formulation process		X	"	A	"
830.1670	Discussion on the formation of impurities		X		A	"
830.1700	Preliminary analysis			NR	NR	
830.1750	Certified limits (158.350)	Standard certified limits	X		A	See CSF dated 12/23/2015 / CLs are standard
		Proposed Limits				
		Justification for wider limits				
830.1800	Enforcement analytical method #		X		A	497997-01 / 497887-13

A = Acceptance, NR = Not Required, G = Data Gap,
W = Waiver Request, I = In Progress, NA = Not Acceptable
# Analytical Method: HPLC method using UV / Photodiode detector set at Wave length: 215 for Permethrin & Pyriproxyfen and 272 nm for Imidacloprid. Validation data have been submitted for accuracy, precision and linearity (MRID: 497997-01 & 497887-13).

8. Group **B:**

Guideline No.	Study Title	Value or Qualitative Description	CITAB's Assessment of Data	MRID Nos.
830.6303	Physical State	Liquid	A	497887-14
830.6314	Oxidation/reduction	NA / does not contain Oxidizing or Reducing agent .	A	"
830.6315	Flammability	Flash point 90°C / Not considered Flammable.	A	"
830.6316	Explodability	Not considered potentially explosive.	A	"
830.6317	Storage stability	Accelerated storage study; All results for 3 actives were with in certified limits.	A	"
830.6310	Miscibility	NA / Not to be diluted with petroleum distillate solvent.	A	"
830.6320	Corrosion characteristics	No signs of corrosion after 2 weeks storage 40° C.	A	"
830.7000	pH	4.98	A	"
830.7100	Viscosity	17.28mm^2 / s (Capillary viscometer)	A	"
830.7300	Density	1.152 g/mL	A	"
830.7520	Particle size	NA / Product does not contain particles or fibres	NA	

A = Acceptable, N = Not Acceptable, G = Data Gap, W = Waiver request, NA = Not applicable, I = In progress

DPBAR CODE NO.: 431150/431027 EPA File Symbol NO.: 91384-G DECISION NO.: 511951
PC Code: 109701,129032,129099 ACTION CODE: R315
FOOD Use: No

CONCLUSIONS:

CITAB has reviewed the product chemistry data submitted/cited for the end-use product and has concluded that:

A. Substantial similarity to the cited product (Reg. No. .....) from Product chemistry view point
[ ] Similar
[ ] Not similar, give reasons
[ ] Identical
[ ] Not identical
[X] Not applicable

B. Confidential Statement of formula

1. Basic CSF (dated: 12/23/2015)
[X] Acceptable
[ ] Not Acceptable
[ ] Not Applicable

If not acceptable provide the reasons

2. Alternate CSF ( )
[ ] Acceptable -
[ ] Not Acceptable -
[X] Not Applicable

If not acceptable give reasons

C. Group A Product Chemistry Data
[X] Acceptable
[ ] Not acceptable
[ ] Acceptable with the exception of Guideline(s): (provide the guideline number & explain)
[ ] Not required
[ ] Data cited

D. Group B Product chemistry data
[X] Acceptable
[ ] Not acceptable
[ ] Acceptable with the exception of Guideline(s): (provide the guideline number & explain)
[ ] Not required
[ ] Data cited

E. Product Label/Draft Label

Recommendations – Yes [ ]; No [X]

If yes, give recommendations below:

Fry, Meridith

From: Richard L. Conn <richard@connsmith.com>
Sent: Wednesday, June 29, 2016 9:49 AM
To: Fry, Meridith
Cc: IVB1; John Tatum
Subject: Re: T2.200 spot-on submission: 91384-G

Hi Meridith,
With this email, on behalf of CAP IM Supply, Inc., I am requesting a two-year conditional time-limited registration for EPA File Symbol 91384-G, which will include the requirement that CAP IM Supply submits quarterly enhanced incident reports and quarterly sales information.

Best regards,
Richard

On 6/23/2016 9:31 AM, Fry, Meridith wrote:

> Good morning Richard,
>
> We are currently reviewing your application for T2.200 For Dogs. With any new pet spot-on product, we are asking registrants to send us an email requesting a two-year conditional, time-limited registration, which includes submission of quarterly enhanced incident reports and quarterly sales information.
>
> We will keep a copy of your email request as part of the product's records. Please let me know if you would be able to send a brief email with this request.
>
> Best regards,
> Meridith
>
> ---
> **Meridith Fry, Ph.D.**
> Acting Product Manager 4
> Invertebrate & Vertebrate Branch 1, S7213
> Registration Division (7505P)
> Office of Pesticide Programs
> U.S. Environmental Protection Agency
> **Email:** Fry.Meridith@epa.gov
> **Phone: 703.347.0128**
> **Fax: 703.305.0204**

--
Richard L. Conn, President, Conn & Smith, Inc.
6713 Catskill Rd, Lorton VA 22079-1113, USA
Phone: (703) 339-4199
http://www.connsmith.com

DATA MATRIX

Date: June 10, 2016	EPA Reg No./File Symbol: 91384-G	Page 1 of 6
Applicant's/Registrant's Name & Address: CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	Product: T2.200 for Dogs	

Ingredient: permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
	SEE SUBSEQUENT PAGES				

Signature: John A. Tatum III/RLC	Name and Title: John A. Tatum III, Chief Operating Officer	Date: 6-10-16

DATA MATRIX

Date: **June 10, 2016**	EPA Reg No./File Symbol: **91384-G**	Page 2 of 6
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Treatments to control pests of humans and pets	49788701	91639	PER	CV-15-143 Pilot study canine flea/tick
810.3300	Treatments to control pests of humans and pets	49788702	91639	PER	CV-15-144 *Ixodes scapularis* (Deer ticks)
810.3300	Treatments to control pests of humans and pets	49788703	91639	PER	CV-15-145 - *Dermacentor variabilis* (American dog ticks)
810.3300	Treatments to control pests of humans and pets	49788704	91639	PER	CV-15-146 - *Rhipicephalus sanguineus* (Brown dog tick)
810.3300	Treatments to control pests of humans and pets	49788705	91639	PER	CV-15-147 - *Amblyomma americanum* (Lone Star tick)
810.3300	Treatments to control pests of humans and pets	49788706	91639	PER	CV-15-148 - *Aedes aegyptii* (mosquitoes)
810.3300	Treatments to control pests of humans and pets	49788707	91639	PER	CV-15-149 - *Stomoxys calcitrans* (biting flies)
810.3300	Treatments to control pests of humans and pets	49788708	91639	PER	CV-15-150 - Waterfastness (repeated water immersion)
810.3300	Treatments to control pests of humans and pets	49788709	91639	PER	CV-15-151 - Ovicidal and larvicidal fleas in dogs
810.3300	Treatments to control pests of humans and pets	49788710	91639	PER	CV-15-152 - Control of fleas in the environment (carpets)
810.3300	Treatments to control pests of humans and pets	49788711	91639	PER	CV-15-153 - Simulated home environment

DATA MATRIX

Date: June 10, 2016	EPA Reg No./File Symbol: 91384-G	Page 3 of 6
Applicant's/Registrant's Name & Address: CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	Product: T2.200 for Dogs	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Treatments to control pests of humans and pets	49788712	91639	PER	Literature review of effic of imidacloprid and permethrin against Chewing Lice, *Trichodectes canis*, infestations on dogs
830.1550	Product identity and composition	49799701	91639	PER	
830.1600	Description of materials used to produce the product	49799701	91639	PER	
830.1650	Description of formulation process	49799701	91639	PER	
830.1670	Discussion of formation of impurities	49799701	91639	PER	
830.1750	Certified limits	49799701	91639	PER	
830.1800	Enforcement analytical method	49799701	91639	PER	
830.6302	Color	49788714	91639	PER	
830.6303	Physical state	49788714	91639	PER	
830.6304	Odor	49788714	91639	PER	
830.6314	Oxidation/reduction: chemical incompatibility				Not applicable -- product does not contain an oxidizing or reducing agent
830.6315	Flammability	49788714	91639	PER	

DATA MATRIX

Date: June 10, 2016	EPA Reg No./File Symbol: 91384-G	Page 4 of 6
Applicant's/Registrant's Name & Address: CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	Product: T2.200 for Dogs	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
830.6316	Explodability				Not applicable -- product not potentially explosive
830.6317	Storage stability	Submitted today	91639	PER	
830.6319	Miscibility				Not applicable -- not an emulsifiable liquied to be diluted with petroleum solvent
830.6320	Corrosion characteristics	Submitted today	91639	PER	
830.6321	Dielectric breakdown voltage				Not applicable -- not to be used around electrical equipment
830.7000	pH	49788714	91639	PER	
830.7100	Viscosity	49788714	91639	PER	
830.7300	Density/relative density/bulk density	49788714	91639	PER	
830.7520	Particle size, fiber length, and diameter distribution				Not applicable -- not a water insoluble substance or fibrous substance
870.1100	Acute oral toxicity	49788715	91639	PER	B-01983 - Acute oral toxicity – Acute toxic class method
870.1200	Acute dermal toxicity	49788716	91639	PER	B-01984 - Acute dermal toxicity

DATA MATRIX

Date: **June 10, 2016**	EPA Reg No./File Symbol: **91384-G**	Page 5 of 6
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.1300	Acute inhalation toxicity				Waiver requested due to product being liquid with low volatility and maximum 4 mL as a single dose to skin of dogs
870.2400	Acute eye irritation	49788717	91639	PER	N-01986 - Non-GLP Acute Eye Irritation / Corrosion
870.2400	Acute eye irritation	49788718	91639	PER	B-01981 - Acute eye irritation / corrosion
870.2500	Acute dermal irritation	49788719	91639	PER	B-01980 - Acute dermal irritation
870.2600	Skin sensitization	49788720	91639	PER	E-01982 - Skin sensitization – Local lymph node assay
870.7200	Companion animal safety	49788721 and 49866901	91639	PER	CV-15-154 - Target Animal Safety Adults (>6 months old)
870.7200	Companion animal safety	49788722 and 49866902	91639	PER	CV-15-155 - Target Animal Safety Puppies (<7 week old)
157.20	Child-resistant packaging testing	48771101	74720	PER	Report KVS-201101
157.20	Child-resistant packaging testing	48703501	74720	PER	Report KVS-201107
157.20	Child-resistant packaging testing	48703502	74720	PER	Report KVS-201108
157.20	Child-resistant packaging testing	48703503	74720	PER	Report KVS-201109
157.20	Child-resistant packaging testing	48703504	74720	PER	Report KVS-201110

DATA MATRIX

Date: June 10, 2016	EPA Reg No./File Symbol: 91384-G	Page 6 of 6
Applicant's/Registrant's Name & Address: CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	Product: T2.200 for Dogs	
Ingredient: permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)		

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
157.20	Child-resistant packaging testing	48652701	74720	PER	Report KVS-201104
157.20	Child-resistant packaging testing	Submitted today	74720	PER	Report KVS-201524
157.20	Child-resistant packaging testing	Submitted today	74720	PER	Report KVS-201525

Certification with Respect to Label Integrity

version: 9/11/02

I certify that the information (including, but not limited to, text, tables, and graphics) contained in the electronic file identified below by file name and submitted with this certification is the same information as that on the paper copies of these documents included with this submission.

PROPOSED LABEL		
EPA Registration #	Date Submitted to EPA	Electronic file name
91384-	June 10, 2016	091384-xxxxx.20160610.T2.200 for Dogs.PDF

I certify that the statements that I have made on this form are true, accurate, and complete. I acknowledge that any knowingly false or misleading statements may be punishable by fine or imprisonment or both under applicable law.

John A. Tatum III/RLC
Signature

6-10-16
Date

John A. Tatum III
Name (typed)

Chief Operating Officer
Title

KLOCKE VERPACKUNGS-SERVICE GMBH

Klocke Verpackungs-Service GmbH Postfach 1140 D-76352 Weingarten

Meredith Fry
Document Processing Desk
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 S. Crystal Drive
Arlington, VA 22202-4501

Phone-No.: 07244/61-1430
EMail-adress: matthias.linder@klocke.com

Contact: Dr. Matthias Linder

Date: 30th May 2016

Letter of Authorization

Dear Sir,

This letter serves to notify you that Klocke Verpackungs-Service GMBH (Klocke), Max-Becker-Str. 6, D-76356 Weingarten, Baden, Germany was the sponsor of certain CRP data. Klocke Verpackungs-Service GMBH owns the data listed in Exhibit A. Klocke Verpackungs-Service GMBH (Klocke) hereby authorizes the U. S. Environmental Protection Agency to allow CAP IM Supply, Inc. located at 303 Perimeter Center North, Suite 300, Atlanta, GA 30346 is authorized to submit or rely upon the following CRP data in support of its registrations of T2.200 for Dogs (EPA Reg. No. 91384-G), pursuant to the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), 7 USC Section 136 et seq.

This authorization is qualified to the extent that:

1) Neither the applicant nor any other person, except the Agency, shall have access to said data unless specifically authorized in writing by Klocke;
2) This authorization does not confer ownership or exclusive rights of the data;
3) This authorization shall not be construed as authorization to use or consider said data, directly or indirectly, in support of any subsequent applications with the exception of any amendment to CAP Supply, Inc.'s registration(s); and
4) This authorization shall not be transferred by the applicant in any manner whatsoever without express prior consent of Klocke.

Insomuch as Klocke is aware of the subject application per 40 CFR 152.116(c) and does not object to the issuance of the registration, the Agency does not need to provide Klocke with the 30-day notification described in paragraph (a) of 40 CFR 152.116.

If you have any questions, please contact our agent, Janelle Kay, Pyxis Regulatory Consulting, Inc. at (253) 853-7369 (Janelle@PyxisRC.com).

Sincerely,

Dr. Matthias Linder, Managing Director
Klocke Verpackungs-Service GMBH
Max-Becker Str. 6
D-76256 Weingarten
Germany
Tel: 49 (7805) 401 115

cc: John Tatum
CAP IM Supply, Inc.

Attachment: Exhibit A

EXHIBIT A

MRID	Reference
48771101	Novosad, M. (2011) Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 0.5 mL Capacity. Project Number: KVS/201101. Unpublished study prepared by National Child Resistant Testing, Inc. 16p.
48703501	Novosad, M. (2011) (Zeronil Spot-On Solution for Dogs): Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 0.67 mL Capacity: (Final Report). Project Number: KVS/201107. Unpublished study prepared by National Child Resistant Testing, Inc. 16p.
48703502	Novosad, M. (2011) (Zeronil Spot-On Solution for Dogs): Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 1.34mL Capacity: (Final Report). Project Number: KVS/201108. Unpublished study prepared by National Child Resistant Testing, Inc. 16p.
48703503	Novosad, M. (2011) (Zeronil Spot-On Solution for Dogs): Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 4.02mL Capacity: (Final Report). Project Number: KSV/201109. Unpublished study prepared by National Child Resistant Testing, Inc. 16p.
48703504	Novosad, M. (2011) (Zeronil Spot-On Solution for Dogs): Child Resistant Packaging Test Summary Report: Thermoforme Blister Pack for Pipettes of 0.5mL Capacity, 067mL Capacity, 1.34mL Capacity, 2.68mL Capacity, 4.02mL Capacity: (Final Report). Project Number: KVS/201110. Unpublished study prepared by National Child Resistant Testing, Inc. 17p.
48652701	Novosad, M. (2011) Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 2.68mL Capacity. Project Number: KVS/201104. Unpublished study prepared by National Child Resistant Testing, Inc. 16p.
	Novosad, M. (2016) Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 0.4 mL Capacity. Project Number: KVS-201524. Unpublished study prepared by National Child Resistant Testing, Inc. 14p.
	Novosad, M. (2016) Child Resistant Packaging Study: Thermoforme Blister Pack for Pipettes of 4.0 mL Capacity. Project Number: KVS-201525. Unpublished study prepared by National Child Resistant Testing, Inc. 14p.

Klocke
Verpackungs-Service GmbH
Max-Becker-Str. 6
D-76356 Weingarten
Fon: 07244/61-0
Fax: 07244/61-1170
Internet: www.klocke.com

Bank Account:
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IBAN: DE81660202860352955442, SWIFT (BIC): HYVEDEMM475
Volksbank Stutensee-Weingarten eG, BLZ 66081724, Kto.-Nr. 30218000
IBAN: DE03660817240030218000, SWIFT (BIC): GENODE61WGA
BW Bank, BLZ 60050101, Kto.-Nr. 4022675
IBAN: DE90600501010004022675, SWIFT (BIC): SOLADEST
Banque Palatine
IBAN: FR7740978000590375033R00148, SWIFT (BIC): BSPFFRPPXXX

Chief Executive Director:
Carsten Klocke / Dr. Matthias Linder
Place of fulfillment: Weingarten/Baden
Place of jurisdiction Karlsruhe
Registration court: district
Mannheim HRB 105401
VAT-ID-no.: DE143584364
Tax no: 34423/20401

CAP IM Supply, Inc.
303 Perimeter Center North, Suite 300
Atlanta, GA 30346

June 10, 2016

Document Processing Desk (REGFEE)
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard Room S-4900
2777 S. Crystal Drive
Arlington, VA 22202

Attention: Meredith Fry, PM Team 4 (Acting), RD

T2.200 for Dogs
EPA File Symbol 91384-G
Change of CRP Packaging from Original Submission

Due to some technical issues with the original packaging we proposed for our T.200 for Dogs product, EPA File Symbol 91384-G, we are changing to a different package type we have previously used under our other company name, CAP Supply, Inc. (EPA Company 91090). In order to adequately support use of that package type for 91384-G, we are today submitting certain new data (CRP test data and accelerated storage/corrosion data), a revised proposed label that reflects new package sizes to correspond to the CRP data available for the new package, and a revised data matrix listing all of the data we are using to support 91384-G.

Data Transmittal
Please consider this letter to be our transmittal document for submission of three copies of the 3 studies listed in the following table:

MRID Number	Study Citation
49947701	McDonnell, A. (2016). Formulation T2: Storage Stability/Corrosion Characteristics in New Packaging. Agenda1 Laboratory Project ID: 160/SS/007. Agenda1 Analytical Services Ltd. 10p.
49947702	Novosad, C. (2016).Child Resistant Packaging Study Thermoforme Blister Pack for Pipettes of 0.4 mL Capacity. Report No. KVS-201524. National Child Resistant Testing, Inc. 14p.
49947703	Novosad, C. (2016).Child Resistant Packaging Study Thermoforme Blister Pack for Pipettes of 4.0 mL Capacity. Report No. KVS-201525. National Child Resistant Testing, Inc. 14p.

Fee for Service
The fee required by the fee for service provisions of FIFRA §33, Category R315, has already been paid and the receipt for payment was included in our December 3, 2015 application package.

Contents of Submission

- Three copies of three data volumes listed on page 1 of this letter
- Revised EPA Form 8570-35, Data Matrix (both Agency Internal Use Copy and Public File Copy)
- Five paper copies of revised proposed label for T2.200 for Dogs
- One copy of the track changes version of the revised proposed label for T2.200 for Dogs
- Certification with Respect to Label Integrity
- One CD bearing PDF of the revised proposed T2.200 for Dogs label
- Authorization letter from Klocke Verpackungs-Service GmbH dated May 30, 2016

If you have any questions, please call me at (801) 512-7543. You may also email me at John.Tatum@CAPSupplyInc.com. You may also interact on all matters regarding this submission with our consultant representative, Richard L. Conn of Conn & Smith, Inc. Mr. Conn's telephone is (703) 339-4199 and his email is richard@connsmith.com.

Sincerely,

John A. Tatum III/RLC

John A. Tatum III
Chief Operating Officer

Enclosures

GREAT LAKES MARKETING RESEARCH

3361 EXECUTIVE PARKWAY, SUITE 201 | TOLEDO, OH 43606
TEL 419.534.4700 | FAX 419.531.7117 | WWW.GLM.COM

LABORATORY ACCREDITATION BUREAU a division of A2LA ACCREDITED ISO/IEC 17025

CRP Data Review for Certification

Prepared For: TruRx
Date: May 13, 2016
Package Identification: 2 mL Safety Tube 0.4 mL fill
GLM Number: Senior Panel 16188

Failure Level	Any senior adult who was unable to open the package within the first five minute test period, or was unable to open the package within the second one minute test period, but was able to pass the screening test, was considered a failure.
Testing Details	At the beginning of each test period, the adult received one 2 mL safety tube filled with 0.4 mL of water. The adult was allowed up to five minutes to familiarize themselves with removing the cap off the tube, breaking the seal and dispensing the water. The second tube the adult received required them to remove the cap off the tube, break the seal and dispense the water within the one minute test period.
Age Distribution	100 seniors: Age 50-54 years 25% (8 males, 17 females) Age 55-59 years 25% (7 males, 18 females), Age 60-70 years 50% (15 males, 35 females)
Access Rate	4 adult failed to open package A 1 adult failed to open package B 1 adult failed to open package B in the required 60 seconds 6 total failures 94% Senior Adult Use Effectiveness
Sites	No site was used for more than 24% of the test
Testers	No single tester tested more than 35% of the panel
Findings	**This test shows that the package described herein satisfies the requirements set forth by 16 CFR 1700**
Data Collected By	Great Lakes Marketing 3361 Executive Parkway Toledo, OH 43606 Lori Mitchell Dixon, PhD, Project Director

GREAT LAKES MARKETING RESEARCH

3361 EXECUTIVE PARKWAY, SUITE 201 | TOLEDO, OH 43606
TEL 419.534.4700 | FAX 419 531 7117 | WWW.GLM.COM

LABORATORY ACCREDITATION BUREAU a division of A-L-B ACCREDITED ISO/IEC 17025

CRP Data Review for Certification

Prepared For: TruRx
Date: May 13, 2016
Package Identification: 2 mL Safety Tube 0.4 mL fill
GLM Number: Child Panel 16188

Failure Level	Any child that was able to gain access to the contents of the tube was considered a failure.
Testing Details	At the beginning of each test period, the child received one 2 mL safety tube filled with 0.4 mL of water.
Age Distribution	50 children: Age 42-44 months 30% (8 males, 7 females) Age 45-48 months 40% (10 males, 10 females) Age 49-51 months 30% (7 males, 8 females)
Access Rate	0 children accessed a package in the first five minutes 1 child accessed a package in the second five minutes 1 child accessed the package during the test First five minutes: 100% Effective Full ten minutes: 98% Effective
Sites	No site was used for more than 20% of the test
Testers	No single tester tested more than 30% of the panel
Findings	**This test shows that the package described herein satisfies the requirements set forth by 16 CFR 1700**
Data Collected By	Great Lakes Marketing 3361 Executive Parkway Toledo, OH 43606 Lori Mitchell Dixon, PhD, Project Director

Fertich, Elizabeth

From: Fertich, Elizabeth
Sent: Tuesday, March 22, 2016 12:21 PM
To: Ciarlo, Timothy
Subject: RE: 91384-G; DP 431031--efficacy technical screen

Thanks!

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Ciarlo, Timothy
Sent: Tuesday, March 22, 2016 12:18 PM
To: Fertich, Elizabeth <fertich.elizabeth@epa.gov>
Subject: RE: 91384-G; DP 431031--efficacy technical screen

Hey Beth,

Sorry about that. Yes, this one passes the tech screen.

Tim

From: Fertich, Elizabeth
Sent: Tuesday, March 22, 2016 12:14 PM
To: Ciarlo, Timothy <Ciarlo.Timothy@epa.gov>
Subject: FW: 91384-G; DP 431031--efficacy technical screen

Hi Tim,
Have you completed the technical screen for this one?
Thanks,
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Saunders, Jennifer
Sent: Tuesday, March 22, 2016 12:07 PM
To: Fertich, Elizabeth <fertich.elizabeth@epa.gov>
Cc: Bohnenblust, Eric <Bohnenblust.Eric@epa.gov>
Subject: RE: 91384-G; DP 431031--efficacy technical screen

Hey Beth, Tim has it!

From: Fertich, Elizabeth
Sent: Tuesday, March 22, 2016 11:57 AM
To: Saunders, Jennifer <Saunders.Jennifer@epa.gov>
Cc: Bohnenblust, Eric <Bohnenblust.Eric@epa.gov>
Subject: 91384-G; DP 431031--efficacy technical screen

Can you please check and see if this is assigned to anyone? The deadline for the technical screen is 3/28 and I want to make sure I don't need to send a 10-day letter for anything efficacy related.
Thanks

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

Conn & Smith Inc.
Professionals in Pesticide Regulatory Services

49866900

March 18, 2016

Document Processing Desk (REGFEE)
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard Room S-4900
2777 S. Crystal Drive
Arlington, VA 22202

Attention: Elizabeth Fertich, IVB1, RD

Submission of Two Companion Animal Report Supplements by Omnipharm Limited (EPA Company 91639) to Support New End Use Product (T2.200 for Dogs) of CAP IM Supply, Inc. (EPA File Symbol 91384-G)

Omnipharm Limited has appointed Conn & Smith, Inc. to act as its agent at EPA. A copy of the appointment letter is enclosed.

The purpose of this submission is for Omnipharm Limited (Omnipharm) to submit a complete response to the study deficiencies identified in your 10-day deficiency letter and review memorandum (DP 431032) that I received from you by email on March 8, 2016. For your convenience I have enclosed a copy of your letter and the review memorandum. To address all of the study deficiencies listed in the February 19, 2016 memorandum by Byron T. Backus for MRID 49788721 (companion animal study in adult dogs) and MRID 49788722 (companion animal study in puppies), Omnipharm Limited is today submitting the enclosed 3 copies of the report supplements listed in the table below. These supplements were prepared by the staff of ClinVet International (Pty) Ltd. Per your request, I am today also sending to you by email these two report supplements as courtesy copies.

Data Transmittal
Please consider this letter to be Omnipharm's transmittal document for submission of three copies of the two study supplements listed in the following table:

MRID Number	Study Citation
49866901	Erasmus, H. (2016). Report Supplement to A Target Animal Safety Study of T2 Applied Topically to Adult Dogs. ClinVet Laboratory Identification Number: CV 15/154. ClinVet International (Pty) Ltd. 253p. Supplement to MRID 49788721. {OCSPP 870.7200}
49866902	Erasmus, H. (2016). Report Supplement to A Target Animal Safety Study of T2 Applied Topically to Puppies. ClinVet Laboratory Identification Number: CV 15/155. ClinVet International (Pty) Ltd. 152p. Supplement to MRID 49788722. {OCSPP 870.7200}

Richard L. Conn
703 • 339 • 4199
richard@connsmith.com

6713 Catskill Road • Lorton, VA 22079-1113 • USA

Cynthia A. Smith
703 • 339 • 1117

If you have any questions, please call me at (703) 339-4199 or you may email me at richard@connsmith.com.

Sincerely,

Richard L. Conn
President
(Agent for Omnipharm Limited)

cc: Martin Donnelly, Omnipharm Limited

Enclosures

BioCity
Pennyfoot Street
Nottingham
United Kingdom
NG1 1GF

March 27th, 2015

Office of Pesticide Programs
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

To Whom It May Concern:

APPOINTMENT OF AUTHORIZED AGENT

Omnipharm Limited, hereby appoints Conn & Smith, Inc., 6713 Catskill Rd, Lorton, VA 22079-1113, to serve as the "authorized agent" of Omnipharm Limited and to act on its behalf on all regulatory matters before the Office of Pesticide Programs (OPP) of the U.S. Environmental Protection Agency. Please mail all OPP correspondence relative to Omnipharm Limited directly to Conn & Smith, Inc. at the Lorton, VA address given in this paragraph.

Sincerely,

Martin Donnelly
Managing Director

Fertich, Elizabeth

From: Fertich, Elizabeth
Sent: Tuesday, March 22, 2016 11:46 AM
To: 'Richard L. Conn'
Cc: John Tatum; David Petrick; 'Martin Donnelly'; IVB1
Subject: RE: Pending product application: EPA File Symbol 91384-G

Richard,
Thanks for providing the electronic copies of the submission. I received all 3 attachments. I will send it off to the toxicity team for review and will contact you if there are additional questions or comments.
Kind regards,
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

From: Richard L. Conn [mailto:richard@connsmith.com]
Sent: Friday, March 18, 2016 3:21 PM
To: Fertich, Elizabeth <fertich.elizabeth@epa.gov>
Cc: John Tatum <John.Tatum@CAPSupplyInc.com>; David Petrick <David.Petrick@CAPInnoVet.com>; 'Martin Donnelly' <martin@sensibleideas.com>
Subject: Re: Pending product application: EPA File Symbol 91384-G

Hi Beth,
I just returned to my office from Document Processing and added the 3-18-16 date pinpunched page to the front of our response cover letter and attachments (the attached file named "91384-G Omnipharm transmittal of supplements to puppy and adult dog studies 3-18-16.pdf"). I will try to attach both both report supplements to this email, but if it bounces back due to exceeding a size limit I will try again by splitting this into two emails to you. The 3 attachments here together constitute a complete copy of what I dropped off at Document Processing around 2:20 PM today.

Hopefully all will be well now with the adult dog and the puppy studies that we submitted to support T2.200 for Dogs, EPA File Symbol 91384-G.

Best regards,
Richard

On 3/11/2016 10:30 AM, Fertich, Elizabeth wrote:

> Hi Richard,
> Thanks for confirming receipt of the letter and review. March 22nd is the deadline for a response and your proposal to send hard copies through front-end processing and provide courtesy copies via email is acceptable. Let me know if you have any questions as you proceed with your response.
>
> Kind regards,
> Beth

Cc: IVB1 <IVB1@epa.gov>
Subject: Pending product application: EPA File Symbol 91384-G

Mr. Conn,
I am working on the pending product application for EPA File Symbol 91384-G. A preliminary review of the companion animal safety study has been completed. Please see the attached deficiency letter and review and respond to my email to confirm receipt. Contact me if you have any questions.

Kind regards,
Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703-347-8560

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Richard L. Conn, President, Conn & Smith, Inc.
6713 Catskill Rd, Lorton VA 22079-1113, USA
Phone: (703) 339-4199
http://www.connsmith.com

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Richard L. Conn, President, Conn & Smith, Inc.
6713 Catskill Rd, Lorton VA 22079-1113, USA
Phone: (703) 339-4199
http://www.connsmith.com

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OPP Decision Number: 511951
EPA File Symbol: 91384-G
Product Name: T2.200 FOR DOGS
EPA Receipt Date: 12/07/2015
EPA Company Number: 91384
Company Name: CAP IM Supply, Inc.

Richard L. Conn
President, Agency for CAP IM Supply, Inc.
Conn and Smith Inc.
6713 Catskill Road
Lorton, VA 22079-1113

Dear Mr. Conn:

The Agency has completed its preliminary technical screening of your application pursuant to Section 33(f)(4)(B)(i)(II) of the Federal Insecticide, Fungicide, and Rodenticide (FIFRA) Act, as amended by the Pesticide Registration Improvement Extension Act. The Agency has determined that your application has not passed the preliminary technical screen and therefore is subject to rejection if the application is not corrected.

Specifically, significant reporting deficiencies (see attached review) have been identified in a screening review of the companion animal safety study in beagle puppies (MRID 49788722). These deficiencies have to be adequately addressed before the study can be fully reviewed.

In order for the review of your product to continue, you will need to correct your application to address the item(s) listed above within 10 business days of the date you received this letter. Corrections must be received by EPA by the 10th business day. EPA recommends sending your complete set of corrections by email to the contact listed below to ensure they are timely received. If studies or confidential information are being submitted by mail, a complete courtesy copy received by email by the deadline will be considered timely. If you cannot correct the application [or do not respond] within 10 business days, your application will be rejected.

At this time you could also choose to withdraw your application. If you have any questions, you may contact Elizabeth Fertich at 703-347-8560 or via email at fertich.elizabeth@epa.gov.

Enclosure: Memorandum: T2.200 FOR DOGS; 91384-G; DP 431032; Decision No. 511951; Action Code R315; Submission No. 978275—Teehnical screen results for companion animal safety study (MRID 49788722).

Sincerely,

Susan Lewis, Director,
Registration Division

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

February 19, 2016

MEMORANDUM:

Subject:	Name of Pesticide Product:	T2.200 FOR DOGS
	EPA Reg. No. /File Symbol:	91384-G
	DP Barcode:	DP 431032
	Decision No.:	511951
	Action Code:	R315
	Submission:	#978275
	PC Codes:	109701 (Permethrin: 44.00%)
		129099 (Imidacloprid: 8.80%)
		129032 (Pyriproxyfen: 0.44%)

From: Byron T. Backus, Ph.D., Toxicologist
CITAB
Registration Division (7505P)

Byron T. Backus
Feb-19-2016

Through: Masih Hashim, Ph.D., Team Leader, Toxicology
CITAB
Registration Division (7505P)

MHashim

To: Elizabeth Fertich
IVB1
Registration Division (7505P)

Registrant: CAP IM SUPPLY, INC.

FORMULATION FROM LABEL:

Active Ingredients:	by wt.
129099 Imidacloprid	8.80%
109701 Permethrin	44.00%
129032 Pyriproxyfen	0.44%
Other Ingredients:	46.76%
TOTAL	100.00%

ACTION REQUESTED: "Please complete a 90-day screen by 3/14/16... Review the submitted companion animal toxicity data and prepare a memo. The following items are attached:

1. cover letter; 2. label; 3. hard copies of studies; 4. data matrix..."

BACKGROUND:

The material received includes a cover letter dated December 3, 2015; a data matrix (dated December 23, 2015) citing two (puppy and adult dog) companion animal safety studies; and a proposed label (proposed dosage rates: 0.4 mL for dogs and puppies weighing 4-10 lbs; 1.0 mL for 11-20 lbs; 2.5 mL for 21-55 lbs; and 4.0 mL for >55 lbs.

COMMENTS AND RECOMMENDATIONS:

1. Significant reporting deficiencies (see below) have been identified in a screening review of the companion animal safety study in beagle puppies (MRID 49788722). These deficiencies have to be adequately addressed before the study can be fully reviewed.

   According to information on page 30 of MRID 49788722, there was a single occurrence of "slight inappetance" (in Group 4 animal 5A2 CBA on Day 1) following administration of the test (or control) substance. "Slight inappetance" is not defined (which is, in itself, a reporting deficiency), although from page 1414 of MRID 49788722 this animal consumed 0-25% (as measured on Day 1) of the food that was offered on Day 0. In a previous report (Study No. 4464) from this laboratory inappetance was defined as consumption of < 25 g dry food/day.

   However (from p. 1414 of MRID 49788722), the same puppy (5A2 CBA) consumed only 0-25% (as measured on Day 11) of the food that was offered on Day 10; from p. 1419 of MRID 49788722 Group 4 puppy 5A4 2FD consumed 0-25% of the food offered on Day 11, from p. 1424 Group 4 puppy 5A7 D8F consumed 0-25% of the food offered on Days 9 and 18, from p. 1426 Group 4 puppy 5A7 E00 (described on p. 30 as listless and with diarrhea on Day 1, but not as showing inappetance) consumed 0-25% of the food offered on Days 0 and 6, from p. 1430 Group 4 puppy 5A8 8F3 consumed 0-25% of the food offered on Day 40. For the control (Group 1) puppies 5A4 191 consumed 0-25% of the food offered on Days 5 and 9 (p. 1384), 5A6 6BA consumed 0-25% on Day 0 (p. 1389), 5A6 AAC consumed 0-25% on Day 13 (p. 1392), 697 FFA consumed 0-25% on Days 0 and 1 (p. 1402) and 0-25% on Day 36 (p. 1403), and 698 0C0 consumed 0-25% on Day 1 (p. 1404). It is concluded that these represent occurrences of inappetance which the summary on page 30 does not report; the summaries should either be corrected or an explanation should be given as to why these incidents should not be a part of these summaries.

An additional concern is that there may be a similar reporting problem with clinical signs. For this reason, all individual twice daily observations (not just occurrences or summarizations of possible adverse effects) should be submitted to the Agency.

From page 23 of MRID 49788722: "The Test/Control Substance was applied topically, divided in two to four spots on the dorsal midline from the shoulders to the base of the tail. All pups weighed less than 9.5 kg and received two spots. Multiple doses were applied in divided doses over a period of no more than two hours to the pups in groups 1 and 4." No information is provided as to how cumulative 5X doses were applied (such as two 2½X doses, or five 1X doses), how much time there was between doses, or whether the application site was allowed to dry between doses. This information should be provided. The report should also state whether the test material to the same site or just the same general area when it was applied multiple times during the space of 2 hours. In addition, draft labeling (submitted December 3, 2015) states (p. 11) that for dogs weighing 4-10 lbs and 11-20 lbs: "Apply the entire contents of the applicator to one spot as shown." This spot would be on the dog's back between the shoulder blades, so there is an inconsistency between the way the test/control materials were applied (to 2 spots) in this study and the directions for use. This inconsistency has to be addressed.

On Day -1 all puppies weighed less than 5 kg so (from dosage rates given on p. 22) it is assumed they all received 2.0 mL (5 x 0.4 mL) of either test or control substance. However, from information on pages 1376 and 1377 one control (male 698 4D1) and two Group 4 (male 5A3 1B0 and female 5C3 CC8) weighed slightly more than 5.0 kg on Day 29 and sbould have each received cumulative doses of 5.0 mL of test/control material on Day 30, which should be confirmed. In addition, it is stated (p. 25) that: "Body weigbts were recorded to two or three decimal points but were rounded up to one decimal point for purposes of dose calculation..." From p. 1377 two Group 4 puppies, female 57B 202 and female 5D1 0EA, weighed 4.91 and 4.94 kg, respectively, on Day 29. The report should state whether these puppies received cumulative doses of 2.0 or 5.0 mL test material on Day 30.

2. A number of deficiencies have been identified in the companion animal safety study in adult beagles (MRID 49788721). These have to be adequately addressed before the study can be fully reviewed.

   Insufficient information was provided regarding administration of the test (or control) substance. From p. 21 of MRID 49788721: "Multiple doses were applied in divided doses over a period of no more than two hours to the dogs in Groups 3 and 4." Additional details should be provided as to how cumulative 3X and 5X doses were applied (such as two 1½X doses for the cumulative 3X, or two 2½X doses for the cumulative 5X), how much time there was between doses, and whether the application site was allowed to dry between doses. The report should also state whether the test material was applied to the same site or just the same general area when it was applied multiple times during the space of 2 hours.

In many cases, the report does not specify the individual dogs which showed signs. On page 33 it is noted that very slight erythema was present in Group 2 dog 5B3 E6F at 1 hour on Day 30, one unidentified dog in Group 3 had very slight erythema on Day 0 at 3 and 4 hours post-administration and on Day 1 at the first observation for the day, and six unidentified Group 4 dogs had very slight erythema on Day 30 at one hour post-administration, and one dog still had slight erythema at 2 and 3 hours post-administration. The report should identify (by animal ID) the dogs that were affected.

The report gives a brief summary (Table H, page 33) of specific post-administration observations. There is no mention of "inappetance." An examination of the individual food consumption data shows (p. 1857) that Group 2 dog DF5 B71 consumed 0-25% of the food offered on Day 0, and (from p. 1888) Group 3 dog CBC 683 consumed 0-25% of the food that was offered on Days 2, 3, 4 and 12, but there is nothing in Table H about these occurrences. As with the puppy study, <u>all</u> individual twice daily observations (not just summarizations of possible adverse effects) should be submitted to the Agency.

Fertich, Elizabeth

From: McAndrew, Eugenia
Sent: Thursday, January 21, 2016 9:47 AM
To: Fertich, Elizabeth
Subject: acute tox screening for 91384-G

Follow Up Flag: Follow up
Due By: Thursday, January 28, 2016 8:00 AM
Flag Status: Flagged

Hi Beth,

The screening for 91384-G is complete. All documents are present. Thank you for sending everything we need.

Jeanie

Jeanie McAndrew
Biologist
Environmental Protection Agency
Office of Chemical Safety and Pollution Prevention
703-308-7051
mcandrew.eugenia@epa.gov

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460
OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION
OFFICE OF PESTICIDE PROGRAMS REGISTRATION DIVISION (7505P)

DP BARCODE No.: 431027; **FILE SYMBOL No.**: 91384-G; **PRODUCT NAME**: T2.200 for Dogs; **DECISION No.**:511951; **PC Code(s)**:129032, 129099, 109701; **ACTION CODE**: R315; **FOOD Use**: No

DATE OUT: January 11, 2016

SUBJECT: 45/90 day screen results for end use product "T2.200 for Dogs"

FROM: Shyam Mathur
Product Chemistry Team Leader
CITAB/RD (7505P)

TO: Elizabeth Fertich / Jennifer Urbanski, RM 04
I-V Branch 1 / RD (7505P)

Company Name: CAP IM Supply Incorporation
Active Ingredient(s): Imidacloprid (8.800%), Pyriproxyfen (0.44%), Permethrin (44.0%)
MRID No(s): 49788713 & 49788714

CONCLUSION:

Deficiencies: No
(if there are deficiencies they are indicated below each heading as Note 1, Note 2 Etc)

Group A: All required data submitted

Group B: All required data submitted

CSF: Basic CSF (dated 12-23-2015) submitted.

Product label: Yes

Note to PM: If the deficiencies are found in the screen results, please inform the registrant and bring back to author of this report the corrected deficiencies in response to 10 day letter. The corrected information will be attached to the original bean, if the data package is still in CITAB. New Bean is required in case the bean has been closed by CITAB. Thank you.

Fertich, Elizabeth

From: Mathur, Shyam
Sent: Monday, January 11, 2016 10:43 AM
To: Fertich, Elizabeth; Urbanski, Jennifer
Cc: Shah, Pv
Subject: 45/90 day screen results for 54287-22 & 91384-G
Attachments: 54287-22 (BOV; alt CSF #3 screen).doc; 91384-G (screen).doc

Follow Up Flag: Follow up
Flag Status: Flagged

Shyam Mathur, Ph. D
Product Chemistry Team Leader
Chemistry, Inert & Toxicology Assessment Branch (CITAB)/RD (7505P)
OCSPP/Environmental Protection Agency, USA
Tel: 703-308-9374
mathur.shyam@epa.gov

CAP IM Supply, Inc.
303 Perimeter Center North, Suite 300
Atlanta, GA 30346

Child Resistant Packaging Certification
For CAP IM Supply, Inc.'s T2.200 for Dogs (EPA File Symbol 91384-G)

Registrant/Applicant: CAP IM Supply, Inc.
303 Perimeter Center North Ste 300
Atlanta, GA 30346

I certify that the packaging that will be used for this product meets the standards of 40 CFR 157.32 including the revised standards in 16 CFR 1700.15(b) when tested by the revised testing procedures in 16 CFR 1700.20 as published in 60 FR 37710 (July 21, 1995).

EPA File Symbol 91384-G, T2.200 for Dogs will be **filled and packaged by Firma Klocke Verpackungs-Service GmbH (KVS)**. The package consists of a filled pipette with a clear plastic front and white foil backing with printing. The clear plastic front lidding is constructed of PET/OPA/ALU/HDPE - 23/25/9/50 mμ) and the forming material for the pipettes is CPA/CPP/COC/HDPE - 50/100/380/50 mμ. This packaging correlates to the ASTM F904 standard. KVS designed and developed a child-resistant package (Thermoforme Applicator) that consists of three or four applicators connected to each other in one strip. There is a perforation between each unit so that a single applicator may be removed from the other two or three units. The applicator is the child-resistant packaging component. The applicator bulbs fall into three different sizes – small, medium, and large – and vary in order to accommodate the different fill volumes. The difference between the three applicator sizes is the bulb end of the applicator which increases in size to accommodate larger volumes. The small applicator is relatively flat and the large applicator is bulbous at the end. Except for the difference in the thickness of the bulb, the overall size of the applicator is identical for all bulb sizes whether combined into strips of 3 units (108 mm x 77 mm) or for strips of 4 units (144 mm x 77 mm). The small applicator fill levels include 0.4 mL and 1.0 mL. The medium applicator fill level is 2.5 mL. The large applicator fill level is 4.0 mL.

I realize that additional Child Resistant Packaging (CRP) testing may be required if EPA File Symbol 91384-G, T2.200 for Dogs is not filled and packaged by KVS on the same equipment as the samples tested. Further, any change in CRP opening instructions from those used in testing, color, size, and/or materials for the CRP may result in additional CRP testing for EPA File Symbol 91384-G, T2.200 for Dogs.

John A. Tatum III
Chief Operating Officer
CAP IM Supply, Inc.

Jan. 7, 2016
Date

Fertich, Elizabeth

From: CAP Innovet <John.Tatum@CAPInnoVet.com>
Sent: Thursday, January 07, 2016 5:49 PM
To: Fertich, Elizabeth
Cc: IVB1; 'Richard L. Conn'
Subject: RE: Pending product application for T2.200 for dogs (EPA file symbol 91384-G)
Attachments: CRP Certification T2.200 for Dogs 91384-G.PDF

Follow Up Flag: Follow up
Flag Status: Flagged

Dear Beth,

Attached is the requested child resistant packaging certification for T2.200 for Dogs (EPA file symbol 91384-G). I hope this meets all the criteria established below for our product package.

Please let us know if you need any additional information.

Thank you,
John

John A. Tatum III - COO
John.Tatum@CAPInnoVet.com
801-512-7543

From: Fertich, Elizabeth [mailto:fertich.elizabeth@epa.gov]
Sent: Wednesday, January 6, 2016 12:39 PM
To: John Tatum <John.Tatum@CAPSupplyInc.com>
Cc: IVB1 <IVB1@epa.gov>
Subject: RE: Pending product application for T2.200 for dogs (EPA file symbol 91384-G)

John,

Please submit a child resistant packaging certification. It should include the following information.

CRP Certification Sample
Notes to Registrant: Put on Company Letterhead

Date:
Subject: Child Resistant Effectiveness/Senior Adult Use Effectiveness Certification
Product Name: XXX
EPA Registration No:

Package Description:

1. Size of package
2. ASTM Classification
3. Closure Name
4. Closure Size
5. Manufacturer

Beth

Elizabeth Fertich
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division (7505P)
Invertebrate and Vertebrate Branch 1 (IVB1)
fertich.elizabeth@epa.gov
703 347-8560

Conn & Smith Inc.
Professionals in Pesticide Regulatory Services

December 23, 2015

Document Processing Desk (REGFEE)
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard Room S-4900
2777 S. Crystal Drive
Arlington, VA 22202

Attention: Kable Bo Davis, PM3, RD

Submission of Replacement Group A Product Chemistry Data Volume by Omnipharm Limited (EPA Company 91639) to Support New End Use Product (T2.200 for Dogs) of CAP IM Supply, Inc. (EPA File Symbol 91384-G)

Omnipharm Limited has appointed Conn & Smith, Inc. to act as its agent at EPA. A copy of the appointment letter is enclosed.

The purpose of this submission is for Omnipharm Limited (Omnipharm) to submit a replacement data volume for Group A product chemistry which has been necessitated by a request during the front end screening of the December 3, 2015 application for new registration of EPA File Symbol 91384-G (T2.200 for Dogs) that was submitted by CAP IM Supply, Inc. Stephanie Varner, Contractor for US EPA, notified CAP IM Supply on December 18 of a need for further information for one of the solvents in the formulation of this product, which had a trade name. The Agency indicated that an acceptable resolution of this matter was the option of removing the trade name and instead using the chemical name only. CAP IM Supply and Omnipharm Limited jointly decided to resolve this EPA request by taking that option which means using a generic version of the solvent in question that does not have a trade name. Since the original Group A data volume had already been processed by EPA, the option of repairing that volume no longer existed, so Omnipharm has prepared the enclosed replacement data volume which will need to have an MRID number assigned to it.

Fee for Service

The fee for service for the proposed new end use product of CAP IM Supply for which the Omnipharm enclosed data are being submitted to support was already paid by CAP IM Supply and the pay.gov receipt was included in their December 3 application for registration.

Richard L. Conn
703 • 339 • 4199
richard@connsmith.com

6713 Catskill Road • Lorton, VA 22079-1113 • USA

Cynthia A. Smith
703 • 339 • 1117
cindy@connsmith.com

Data Transmittal

Please consider this letter to be Omnipharm's transmittal document for submission of three copies of the study listed in the following table:

MRID Number	Study Citation
49799701	Donnelly, M. (2015). Formulation T2: Group A - Product Identity, Composition, and Analysis. Omnipharm Limited. 112p. {OCSPP 830.1550, 830.1600, 830.1650, 830.1670, 830.1700, 830.1750, 830.1800}

If you have any questions, please call me at (703) 339-4199 or you may email me at richard@connsmith.com.

Sincerely,

Richard L. Conn
President
(Agent for Omnipharm Limited)

cc: Martin Donnelly, Omnipharm Limited

Enclosures

BioCity
Pennyfoot Street
Nottingham
United Kingdom
NG1 1GF

March 27th, 2015

Office of Pesticide Programs
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

To Whom It May Concern:

APPOINTMENT OF AUTHORIZED AGENT

Omnipharm Limited, hereby appoints Conn & Smith, Inc., 6713 Catskill Rd, Lorton, VA 22079-1113, to serve as the "authorized agent" of Omnipharm Limited and to act on its behalf on all regulatory matters before the Office of Pesticide Programs (OPP) of the U.S. Environmental Protection Agency. Please mail all OPP correspondence relative to Omnipharm Limited directly to Conn & Smith, Inc. at the Lorton, VA address given in this paragraph.

Sincerely,

Martin Donnelly
Managing Director

CAP IM Supply, Inc.
303 Perimeter Center North, Suite 300
Atlanta, GA 30346

December 23, 2015

Document Processing Desk (REGFEE)
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard Room S-4900
2777 S. Crystal Drive
Arlington, VA 22202

Attention: Kable Bo Davis, PM3, RD

T2.200 for Dogs
EPA File Symbol 91384-G
Replacement Forms 8570-4, 8570-27, and 8570-35

During front-end processing of EPA File Symbol 91384-G, T2.200 for Dogs, the Agency (through Stephanie Varner, Contractor, US EPA) requested further information for one of the solvents in the formulation which used a specific trade name. In the interest of saving time, CAP IM Supply, Inc. decided to resolve the request by changing to a generic source of that solvent which does not have a trade name, and therefore EPA Form 8570-4 (Confidential Statement of Formula) submitted herein now shows only the chemical name of the solvent in question.

To fully accommodate that source change, we are enclosing two original signature copies of an updated 8570-4 form dated December 23, 2015, a revised EPA Form 8570-27 that reflects that new date of the 8570-4 form, and both the Agency and Public versions of the Data Matrix (EPA Form 8570-35) which are dated December 23, 2015 and show a December 23, 2015 submission by Omnipharm Limited to satisfy the Group A product chemistry requirements. The Group A product chemistry data volume was modified from the one submitted December 3, 2015 to reflect the generic source of the solvent referred to above. As a result of these changes, the original Group A product chemistry data volume that Omnipharm Limited submitted December 3, 2015 should not be used when the data supporting EPA File Symbol 91384-G are reviewed. EPA has not provided any MRID numbers to date for the December 3 submission.

Fee for Service
The fee required by the fee for service provisions of FIFRA §33, Category R315, has already been paid and the receipt for payment was included in our December 3, 2015 application package.

If you have any questions, please call me at (801) 512-7543. You may also email me at John.Tatum@CAPSupplyInc.com. You may also interact on all matters regarding this submission with our consultant representative, Richard L. Conn of Conn & Smith, Inc. Mr. Conn's telephone is (703) 339-4199 and his email is richard@connsmith.com.

Sincerely,

John A. Tatum III /RLC

John A. Tatum III
Chief Operating Officer

Enclosures

Form Approved. OMB No. 2070-0060. Approval Expires 11-30 93

United States Environmental Protection Agency
Washington,DC 20460

Formulator's Exemption Statement

(40 CFR 152. 85)

Applicant's Name and Address	EPA File Symbol/Registration Number
CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	91384-G
	Product Name T2.200 for Dogs
	Date of Confidential Statement of Formula *(EPA Form 8570-4)* December 23, 2015

As an authorized representative of the applicant for registration of the product identified above, I here certify that:

(1) This product contains the following active ingredient(s):

permethrin, imidacloprid and pyriproxyfen

(2) Of these, each active ingredient listed in paragraph (4) is present solely as the result of the use of that active ingredient in the manufacturing, formulation or repackaging of another product which contains that active ingredient, which is registered under FIFRA Section 3, is purchased by us from another producer, and is labeled for at least each use for which my product is proposed to be labeled.

(3) Indicate by checking (A) or (B) below which paragraph applies:

☒ (A) An accurate Confidential Statement of Formula *(EPA Form 8570-4)* for the above identified product is attached to this statement. That formula statement indicate, by company name, registration number, and product name, the source of the active ingredient(s) listed in paragraph (1).

OR

☐ (B) The Confidential Statement of Formula *(CSF) (EPA Form 8570-4)* referenced above and on file with the EPA is complete, current, and accurate and contains the information required on the current CSF.

(4) The following active ingredients in this product qualify for the formulator's exemption.

	Source	
Active Ingredient	Product Name	Registration Number
permethrin	[redacted]	[redacted]
imidacloprid		
pyriproxyfen		

Signature	Name and Title	Date
John A. Tatum III/RLC	John A. Tatum III Chief Operating Officer	12-23-15

EPA Form 8570-27 (Rev. 7-91) White - EPA copy Yellow - Applicant copy

Product ingredient source information may be entitled to confidential treatment

DATA MATRIX

Date: **December 23, 2015**	EPA Reg No./File Symbol: **91384-G**	Page 1 of 6
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
	SEE SUBSEQUENT PAGES				

Signature: John A. Tatum III/RLC	Name and Title: John A. Tatum III, Chief Operating Officer	Date: 12-23-15

DATA MATRIX

Date: **December 23, 2015**	EPA Reg No./File Symbol: **91384-G**	Page 2 of 6
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-143 Pilot study canine flea/tick
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-144 *Ixodes scapularis* (Deer ticks)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-145 - *Dermacentor variabilis* (American dog ticks)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-146 - *Rhipicephalus sanguineus* (Brown dog tick)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-147 - *Amblyomma americanum* (Lone Star tick)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-148 - *Aedes aegyptii* (mosquitoes)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-149 - *Stomoxys calcitrans* (biting flies)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-150 - Waterfastness (repeated water immersion)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-151 - Ovicidal and larvicidal fleas in dogs
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-152 - Control of fleas in the environment (carpets)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-153 - Simulated home environment

DATA MATRIX

Date: **December 23, 2015**	EPA Reg No./File Symbol: **91384-G**	Page 3 of 6
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	Literature review of effi of imidacloprid and permethrin against Chewing Lice, *Trichodectes canis* , infestations on dogs
830.1550	Product identity and composition	Submitted Dec 23, 2015	91639	PER	
830.1600	Description of materials used to produce the product	Submitted Dec 23, 2015	91639	PER	
830.1650	Description of formulation process	Submitted Dec 23, 2015	91639	PER	
830.1670	Discussion of formation of impurities	Submitted Dec 23, 2015	91639	PER	
830.1750	Certified limits	Submitted Dec 23, 2015	91639	PER	
830.1800	Enforcement analytical method	Submitted Dec 23, 2015	91639	PER	
830.6302	Color	Submitted Dec 3, 2015	91639	PER	
830.6303	Physical state	Submitted Dec 3, 2015	91639	PER	
830.6304	Odor	Submitted Dec 3, 2015	91639	PER	
830.6314	Oxidation/reduction: chemical incompatibility				Not applicable -- product does not contain an oxidizing or reducing agent
830.6315	Flammability	Submitted Dec 3, 2015	91639	PER	

DATA MATRIX

Date: December 23, 2015	EPA Reg No./File Symbol: 91384-G	Page 4 of 6
Applicant's/Registrant's Name & Address: CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	Product: T2.200 for Dogs	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
830.6316	Explodability				Not applicable -- product not potentially explosive
830.6317	Storage stability	Submitted Dec 3, 2015	91639	PER	
830.6319	Miscibility				Not applicable -- not an emulsifiable liquied to be diluted with petroleum solvent
830.6320	Corrosion characteristics	Submitted Dec 3, 2015	91639	PER	
830.6321	Dielectric breakdown voltage				Not applicable -- not to be used around electrical equipment
830.7000	pH	Submitted Dec 3, 2015	91639	PER	
830.7100	Viscosity	Submitted Dec 3, 2015	91639	PER	
830.7300	Density/relative density/bulk density	Submitted Dec 3, 2015	91639	PER	
830.7520	Particle size, fiber length, and diameter distribution				Not applicable -- not a water insoluble substance or fibrous substance
870.1100	Acute oral toxicity	Submitted Dec 3, 2015	91639	PER	B-01983 - Acute oral toxicity – Acute toxic class method
870.1200	Acute dermal toxicity	Submitted Dec 3, 2015	91639	PER	B-01984 - Acute dermal toxicity

DATA MATRIX

Date: **December 23, 2015**	EPA Reg No./File Symbol: **91384-G**	Page 5 of 6
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.1300	Acute inhalation toxicity				Waiver requested due to product being liquid with low volatility and maximum 4 mL as a single dose to skin of dogs
870.2400	Acute eye irritation	Submitted Dec 3, 2015	91639	PER	N-01986 - Non-GLP Acute Eye Irritation / Corrosion
870.2400	Acute eye irritation	Submitted Dec 3, 2015	91639	PER	B-01981 - Acute eye irritation / corrosion
870.2500	Acute dermal irritation	Submitted Dec 3, 2015	91639	PER	B-01980 - Acute dermal irritation
870.2600	Skin sensitization	Submitted Dec 3, 2015	91639	PER	E-01982 - Skin sensitization – Local lymph node assay
870.7200	Companion animal safety	Submitted Dec 3, 2015	91639	PER	CV-15-154 - Target Animal Safety Adults (>6 months old)
870.7200	Companion animal safety	Submitted Dec 3, 2015	91639	PER	CV-15-155 - Target Animal Safety Puppies (<7 week old)
157.20	Child-resistant packaging testing	49649301	74720	PER	Report KVS-201501
157.20	Child-resistant packaging testing	49649305	74720	PER	Report KVS-201505
157.20	Child-resistant packaging testing	49649308	74720	PER	Report KVS-201508
157.20	Child-resistant packaging testing	49649309	74720	PER	Report KVS-201509
157.20	Child-resistant packaging testing	49649310	74720	PER	Report KVS-201510

DATA MATRIX

Date: **December 23, 2015**	EPA Reg No./File Symbol: **91384-G**	Page 6 of 6
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
157.20	Child-resistant packaging testing	49649313	74720	PER	Report KVS-201513
157.20	Child-resistant packaging testing	49681401	74720	PER	Report KVS-201514
157.20	Child-resistant packaging testing	49681402	74720	PER	Report KVS-201515
157.20	Child-resistant packaging testing	49681403	74720	PER	Report KVS-201516
157.20	Child-resistant packaging testing	49719401	74720	PER	Report KVS-201517
157.20	Child-resistant packaging testing	49719402	74720	PER	Report KVS-201518
157.20	Child-resistant packaging testing	49719403	74720	PER	Report KVS-201521

DATA MATRIX

Date: **December 23, 2015**	EPA Reg No./File Symbol: **91384-G**
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]			SEE SUBSEQUENT PAGES		

Signature: John A. Tatum III/RLC	Name and Title: John A. Tatum III, Chief Operating Officer	Date: 12-23-15

DATA MATRIX

Date: December 23, 2015

EPA Reg No./File Symbol: 91384-G

Applicant's/Registrant's Name & Address:
CAP IM Supply, Inc.
303 Perimeter Center North Ste 300
Atlanta, GA 30346

Product:
T2.200 for Dogs

Ingredient: permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]			91639	PER	CV-15-143 Pilot study canine flea/tick
			91639	PER	CV-15-144 *Ixodes scapularis* (Deer ticks)
			91639	PER	CV-15-145 - *Dermacentor variabilis* (American dog ticks)
			91639	PER	CV-15-146 - *Rhipicephalus sanguineus* (Brown dog tick)
			91639	PER	CV-15-147 - *Amblyomma americanum* (Lone Star tick)
			91639	PER	CV-15-148 - *Aedes aegyptii* (mosquitoes)
			91639	PER	CV-15-149 - *Stomoxys calcitrans* (biting flies)
			91639	PER	CV-15-150 - Waterfastne. (repeated water immersion)
			91639	PER	CV-15-151 - Ovicidal and larvicidal fleas in dogs
			91639	PER	CV-15-152 - Control of fleas in the environment (carpets)
			91639	PER	CV-15-153 - Simulated home environment

DATA MATRIX

Date: December 23, 2015	EPA Reg No./File Symbol: 91384-G	Page 3 of 6
Applicant's/Registrant's Name & Address: CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	Product: T2.200 for Dogs	

Ingredient: permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]			91639	PER	Literature review of effi of imidacloprid and permethrin against Chewing Lice, *Trichodectes canis* , infestations on dogs
			91639	PER	
			91639	PER	
			91639	PER	
			91639	PER	
			91639	PER	
			91639	PER	
			91639	PER	
			91639	PER	
			91639	PER	
			91639	PER	
					Not applicable -- product does not contain an oxidizing or reducing agent
			91639	PER	

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Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]					Not applicable -- product not potentially explosive
			91639	PER	
					Not applicable -- not an emulsifiable liquied to be diluted with petroleum solvent
			91639	PER	
					Not applicable -- not to be used around electrical equipment
			91639	PER	
			91639	PER	
			91639	PER	
					Not applicable -- not a water insoluble substance or fibrous substance
			91639	PER	B-01983 - Acute oral toxicity – Acute toxic class method
			91639	PER	B-01984 - Acute dermal toxicity

DATA MATRIX

Date: December 23, 2015	EPA Reg No./File Symbol: 91384-G	Page 5 of 6
Applicant's/Registrant's Name & Address: CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	Product: T2.200 for Dogs	

Ingredient: permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]					Waiver requested due to product being liquid with low volatility and maximum 4 mL as a single dose to skin of dogs
			91639	PER	N-01986 - Non-GLP Acute Eye Irritation / Corrosion
			91639	PER	B-01981 - Acute eye irritation / corrosion
			91639	PER	B-01980 - Acute dermal irritation
			91639	PER	E-01982 - Skin sensitization – Local lymph node assay
			91639	PER	CV-15-154 - Target Animal Safety Adults (>6 months old)
			91639	PER	CV-15-155 - Target Animal Safety Puppies (<7 week old)
			74720	PER	Report KVS-201501
			74720	PER	Report KVS-201505
			74720	PER	Report KVS-201508
			74720	PER	Report KVS-201509
			74720	PER	Report KVS-201510

DATA MATRIX

Date: **December 23, 2015**	EPA Reg No./File Symbol: **91384-G** Page 6 of 6
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**
Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**	

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			74720	PER	Report KVS-201513
			74720	PER	Report KVS-201514
			74720	PER	Report KVS-201515
			74720	PER	Report KVS-201516
			74720	PER	Report KVS-201517
			74720	PER	Report KVS-201518
			74720	PER	Report KVS-201521

Conn & Smith Inc.
Professionals in Pesticide Regulatory Services

December 3, 2015

Document Processing Desk (REGFEE)
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard Room S-4900
2777 S. Crystal Drive
Arlington, VA 22202

Attention: Kable Bo Davis, PM3, RD

Submission of Data by Omnipharm Limited (EPA Company 91639) to Support New End Use Product (T2.200 for Dogs) of CAP IM Supply, Inc. (EPA Company 91384)

Omnipharm Limited has appointed Conn & Smith, Inc. to act as its agent at EPA. A copy of the appointment letter is enclosed.

The purpose of this submission is for Omnipharm Limited (Omnipharm) to submit the studies identified below to support the application for registration of a new end use product, T2.200 for Dogs, being submitted to EPA today from CAP IM Supply, Inc. (CAP IM Supply). Omnipharm has provided a letter of authorization to CAP IM Supply which CAP IM Supply has included in its applications for registration that permits EPA to reply upon the enclosed Omnipharm data. It is important to note that Omnipharm is not submitting its own application for registration - it is only submitting the enclosed data that will be used to support CAP IM Supply application for registration of T2.200 for Dogs.

Please note that the study reports enclosed all refer to the test substance as "T2" which is the abbreviation Omnipharm and the testing facilities have used during the data development phase of this registration project to represent the formulation for which CAP IM Supply is seeking registration. The three active ingredients in the T2 formulation are permethrin at 44.00%, imidacloprid at 8.80% and pyriproxyfen at 0.44%. The test substance referred to as "T2" in these study reports has the same formulation as T2.200 for Dogs, for which CAP IM Supply is seeking EPA registration.

Fee for Service
The fees for service for the proposed new end use product of CAP IM Supply for which the Omnipharm enclosed data are being submitted to support have been paid by CAP IM Supply and its submission includes the pay.gov receipt for their application for registration.

Data Transmittal
Please consider this letter to be Omnipharm's transmittal document for submission of three copies of the 22 studies listed in the following table:

Richard L. Conn
703 • 339 • 4199
richard@connsmith.com

6713 Catskill Road • Lorton, VA 22079-1113 • USA

Cynthia A. Smith
703 • 339 2237
cindy@connsmith.com

MRID Number	Study Citation
49788701	Erasmus, H. (2015). A pilot study to assess the local tolerance and efficacy of T2 formulation against ticks (Rhipicephalus sanguineus) and fleas (Ctenocephalides felis) on dogs. ClinVet Laboratory Identification Number: CV 15/143. ClinVet International (Pty) Ltd. 95p.
49788702	Liebenberg, J. (2015). A dose confirmation of T2 formulation against artificial infestations of adult ticks (Ixodes scapularis) on dogs. ClinVet Laboratory Identification Number: CV 15/144. ClinVet International (Pty) Ltd. 107p. {OCSPP 810.3300}
49788703	de Vos, C. (2015). A Dose Confirmation of T2 Formulation Against Artificial Infestations of Ticks (Dermacentor variabilis) on Dogs. ClinVet Laboratory Identification Number: CV 15/145. ClinVet International (Pty) Ltd. 94p. {OCSPP 810.3300}
49788704	Neethling, W. (2015). A dose confirmation of T2 formulation against artificial infestations of ticks (Rhipicephalus sanguineus) and fleas (Ctenocephalides felis) on dogs. ClinVet Laboratory Identification Number: CV 15/146. ClinVet International (Pty) Ltd. 117p. {OCSPP 810.3300}
49788705	Liebenberg, J. (2015). A dose confirmation of T2 formulation against artificial infestations of ticks (Amblyomma americanum) on dogs. ClinVet Laboratory Identification Number: CV 15/147. ClinVet International (Pty) Ltd. 101p. {OCSPP 810.3300}
49788706	Neethling, W. (2015). A Dose Confirmation of the Efficacy of T2 Formulation Against Mosquitoes on Dogs Experimentally Exposed to Aedes aegypti. ClinVet Laboratory Identification Number: CV 15/148. ClinVet International (Pty) Ltd. 131p. {OCSPP 810.3300}
49788707	de Vos, C. (2015). A dose confirmation of T2 formulation against artificial infestations of stable flies (Stomoxys calcitrans) and onset of efficacy of T2 formulation against fleas (Ctenocephalides felis) on dogs. ClinVet Laboratory Identification Number: CV 15/149. ClinVet International (Pty) Ltd. 183p. {OCSPP 810.3300}

MRID Number	Study Citation
49788708	de Vos, C. (2015). A study to determine the effect of water immersion and shampooing on the efficacy of T2 against fleas (Ctenocephalides felis) on dogs. ClinVet Laboratory Identification Number: CV 15/150. ClinVet International (Pty) Ltd. 107p. {OCSPP 810.3300}
49788709	de Vos, C. (2015). Efficacy Study of T2 Against the Further Development of Flea (Ctenocephalides felis) Eggs Collected from Dogs Infested with Gravid Fleas. ClinVet Laboratory Identification Number: CV 15/151. ClinVet International (Pty) Ltd. 106p. {OCSPP 810.3300}
49788710	Neethling, W. (2015). A study to assess the efficacy of T2 formulation to control fleas (Ctenocephalides felis) in a dog's environment through assessing flea egg development in vitro on carpet samples. ClinVet Laboratory Identification Number: CV 15/152. ClinVet International (Pty) Ltd. 99p. {OCSPP 810.3300}
49788711	Neethling, W. (2015). A Randomised, Negative Controlled Study Assessing the Efficacy of Formulation T2 in the Prevention of Flea (Ctenocephalides felis) Infestations on Dogs in a Simulated Home Environment. ClinVet Laboratory Identification Number: CV 15/153. ClinVet International (Pty) Ltd. 115p. {OCSPP 810.3300}
49788712	Meyer, J. (2015). Review of Scientific Literature Associated with Efficacy of Imidacloprid and Permethrin against Chewing Lice, Trichodectes canis, Infestations on Dogs. Triveritas Ltd. 7p. {OCSPP 810.3300}
49788713	Donnelly, M. (2015). Formulation T2: Group A - Product Identity, Composition, and Analysis. Omnipharm Limited. 111p. {OCSPP 830.1550, 830.1600, 830.1650, 830.1670, 830.1700, 830.1750, 830.1800}

MRID Number	Study Citation
49788714	Donnelly, M. (2015). Formulation T2: Physical-Chemical Characteristics. Omnipharm Limited. 29p. {OCSPP 830.6302, 830.6303, 830.6304, 830.6313, 830.6314, 830.6315, 830.6316, 830.6317, 830.6319, 830.6320, 830.6321, 830.7000, 830.7050, 830.7100, 830.7200, 830.7220, 830.7300, 830.7370, 830.7520, 830.7550, 830.7840, 830.7950}
49788715	Ordonez, P. (2015). Final Report: Evaluation of the acute oral toxicity of the test item *T2 formulation* in female Sprague Dawley rats by the up-and-down testing procedure. Laboratory Project ID B-01983. Vivotecnia Research S.L. 86p. {OCSPP 870.1100}
49788716	Ordonez, P. (2015). Final Report: Evaluation of the acute dermal toxicity of the test item *T2 formulation* after a single dose administration to male and female Sprague Dawley rats. Laboratory Project ID B-01984. Vivotecnia Research S.L. 67p. {OCSPP 870.1200}
49788717	Ordonez, P. (2015). Final Report: Evaluation of the acute ocular irritant and/or corrosive effect of the test item *T2* after a single dose administration to female *New Zealand White* rabbits. Laboratory Project ID N-01986. Vivotecnia Research S.L. 92p. {OCSPP 870.2400}
49788718	Ordonez, P. (2015). Final Report: Evaluation of the acute ocular irritant and/or corrosive effect of the test item *T2 formulation* after a single dose administration to female *New Zealand White* rabbits. Laboratory Project ID B-01976. Vivotecnia Research S.L. 83p. {OCSPP 870.2400}
49788719	Ordonez, P. (2015). Final Report: Evaluation of the acute dermal irritant and/or corrosive effect of the test item *T2 formulation* after a single dose administration to female New Zealand White rabbits. Laboratory Project ID B-01980. Vivotecnia Research S.L. 71p. {OCSPP 870.2500}
49788720	Leoni, A. (2015). Test for Sensitization (Local Lymph Node Assay - LLNA) with T2. BSL Study Number: 153780. BSL BIOSERVICE Scientific Laboratories GmbH. 53p. {OCSPP 870.2600}

MRID Number	Study Citation
49788721	Erasmus, H. (2015). A Target Animal Safety Study of T2 Applied Topically to Adult Dogs. ClinVet Laboratory Identification Number: CV 15/154. ClinVet International (Pty) Ltd. 1963p. {OCSPP 870.7200}
49788722	Erasmus, H. (2015). A Target Animal Safety Study of T2 Applied Topically to Puppies. ClinVet Laboratory Identification Number: CV 15/155. ClinVet International (Pty) Ltd. 1479p. {OCSPP 870.7200}

If you have any questions, please call me at (703) 339-4199 or you may email me at richard@connsmith.com.

Sincerely,

Richard L. Conn
President
(Agent for Omnipharm Limited)

cc: Martin Donnelly, Omnipharm Limited

Enclosures

BioCity
Pennyfoot Street
Nottingham
United Kingdom
NG1 1GF

March 27th, 2015

Office of Pesticide Programs
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

To Whom It May Concern:

APPOINTMENT OF AUTHORIZED AGENT

Omnipharm Limited, hereby appoints Conn & Smith, Inc., 6713 Catskill Rd, Lorton, VA 22079-1113, to serve as the "authorized agent" of Omnipharm Limited and to act on its behalf on all regulatory matters before the Office of Pesticide Programs (OPP) of the U.S. Environmental Protection Agency. Please mail all OPP correspondence relative to Omnipharm Limited directly to Conn & Smith, Inc. at the Lorton, VA address given in this paragraph.

Sincerely,

Martin Donnelly
Managing Director

21-Day Screen Completed by Contractor

21-Day Expires on 12-28-15

Jacket # 91384-G
MRID# 497887

Content Screen: Recommend to Pass/Fail

11-3 Review: Pass/Fail/NA

Overall Status: Recommend to Pass/Fail

Transfer This Jacket to:

STEPHEN SCHAICBE

Form Approved. OMB No. 2070-0060. Approval Expires 11-30 93

United States Environmental Protection Agency
Washington, DC 20460

Formulator's Exemption Statement

(40 CFR 152. 85)

Applicant's Name and Address	EPA File Symbol/Registration Number
CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	91384- Product Name T2.200 for Dogs Date of Confidential Statement of Formula *(EPA Form 8570-4)* DECEMBER 3, 2015

As an authorized representative of the applicant for registration of the product identified above, I here certify that:

(1) This product contains the following active ingredient(s):

permethrin, imidacloprid and pyriproxyfen

(2) Of these, each active ingredient listed in paragraph (4) is present solely as the result of the use of that active ingredient in the manufacturing, formulation or repackaging of another product which contains that active ingredient, which is registered under FIFRA Section 3, is purchased by us from another producer, and is labeled for at least each use for which my product is proposed to be labeled.

(3) Indicate by checking (A) or (B) below which paragraph applies:

☒ (A) An accurate Confidential Statement of Formula *(EPA Form 8570-4)* for the above identified product is attached to this statement. That formula statement indicate, by company name, registration number, and product name, the source of the active ingredient(s) listed in paragraph (1).

OR

☐ (B) The Confidential Statement of Formula *(CSF) (EPA Form 8570-4)* referenced above and on file with the EPA is complete, current, and accurate and contains the information required on the current CSF.

(4) The following active ingredients in this product qualify for the formulator's exemption.

	Source	
Active Ingredient	Product Name	Registration Number
permethrin	[redacted]	
imidacloprid		
pyriproxyfen		

Signature	Name and Title	Date
	John A. Tatum III Chief Operating Officer	12-3-15

EPA Form 8570-27 (Rev. 7-91) White - EPA copy Yellow - Applicant copy

Product ingredient source information may be entitled to confidential treatment

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 1.25 hours per response for registration and 0.25 hours per response for reregistration and special review activities, including time for reading the instructions and completing the necessary forms. Send comments regarding burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460.
Do not send the completed form to this address.

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number	EPA Registration Number/File Symbol
CAP IM Supply, Inc., 303 Perimeter Center North Ste 300, Atlanta, GA 30346 (801) 512-7543	91384-
Active Ingredient(s) and/or representative test compound(s): permethrin, imidacloprid, pyriproxyfen	Date: 12-3-15
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158): indoor nonfood	Product Name: T2.200 for Dogs

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I- METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

☒ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of deta requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements]

☐ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this epplication, to the extent required by FIFRA.

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all deta submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identicel or similar composition and uses .

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original deta submitter or that I have obtained the written permission of the originel data submitter to cite that study.

I certify that for each study cited in support of this registretion or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (1) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify thet in all instances where an offer of compensation is required, copies of ell offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency mey initiate action to deny, cancel or suspend the registretion of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
[signature]	12-3-15	John A. Tatum III, Chief Operating Officer

EPA Form 8570-34 (9-97) Electronic and Paper versions available. Submit only Paper version.

DATA MATRIX

Date: December 3, 2015	EPA Reg No./File Symbol: 91384-	Page 1 of 6
Applicant's/Registrant's Name & Address: CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	Product: T2.200 for Dogs	

Ingredient: permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
	SEE SUBSEQUENT PAGES				

Signature:	Name and Title: John A. Tatum III, Chief Operating Officer	Date: 12-3-15

DATA MATRIX

Date: December 3, 2015	EPA Reg No./File Symbol: 91384-	Page 2 of 6
Applicant's/Registrant's Name & Address: CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	Product: T2.200 for Dogs	

Ingredient: permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-143 Pilot study canine flea/tick
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-144 *Ixodes scapularis* (Deer ticks)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-145 - *Dermacentor variabilis* (American dog ticks)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-146 - *Rhipicephalus sanguineus* (Brown dog tick)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-147 - *Amblyomma americanum* (Lone Star tick)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-148 - *Aedes aegyptii* (mosquitoes)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-149 - *Stomoxys calcitrans* (biting flies)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-150 - Waterfastness (repeated water immersion)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-151 - Ovicidal and larvicidal fleas in dogs
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-152 - Control of fleas in the environment (carpets)
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	CV-15-153 - Simulated home environment

DATA MATRIX

Date: **December 3, 2015**	EPA Reg No./File Symbol: **91384-**	Page 3 of 6
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Treatments to control pests of humans and pets	Submitted Dec 3, 2015	91639	PER	Literature review of eff of imidacloprid and permethrin against Chewing Lice, *Trichodectes canis*, infestations on dogs
830.1550	Product identity and composition	Submitted Dec 3, 2015	91639	PER	
830.1600	Description of materials used to produce the product	Submitted Dec 3, 2015	91639	PER	
830.1650	Description of formulation process	Submitted Dec 3, 2015	91639	PER	
830.1670	Discussion of formation of impurities	Submitted Dec 3, 2015	91639	PER	
830.1750	Certified limits	Submitted Dec 3, 2015	91639	PER	
830.1800	Enforcement analytical method	Submitted Dec 3, 2015	91639	PER	
830.6302	Color	Submitted Dec 3, 2015	91639	PER	
830.6303	Physical state	Submitted Dec 3, 2015	91639	PER	
830.6304	Odor	Submitted Dec 3, 2015	91639	PER	
830.6314	Oxidation/reduction: chemical incompatibility				Not applicable -- product does not contain an oxidizing or reducing agent
830.6315	Flammability	Submitted Dec 3, 2015	91639	PER	

DATA MATRIX

Date: **December 3, 2015**	EPA Reg No./File Symbol: **91384-**	Page 4 of 6
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
830.6316	Explodability				Not applicable -- product not potentially explosive
830.6317	Storage stability	Submitted Dec 3, 2015	91639	PER	
830.6319	Miscibility				Not applicable -- not an emulsifiable liquied to be diluted with petroleum solvent
830.6320	Corrosion characteristics	Submitted Dec 3, 2015	91639	PER	
830.6321	Dielectric breakdown voltage				Not applicable -- not to be used around electrical equipment
830.7000	pH	Submitted Dec 3, 2015	91639	PER	
830.7100	Viscosity	Submitted Dec 3, 2015	91639	PER	
830.7300	Density/relative density/bulk density	Submitted Dec 3, 2015	91639	PER	
830.7520	Particle size, fiber length, and diameter distribution				Not applicable -- not a water insoluble substance or fibrous substance
870.1100	Acute oral toxicity	Submitted Dec 3, 2015	91639	PER	B-01983 - Acute oral toxicity – Acute toxic class method
870.1200	Acute dermal toxicity	Submitted Dec 3, 2015	91639	PER	B-01984 - Acute dermal toxicity

DATA MATRIX

Date: December 3, 2015	EPA Reg No./File Symbol: 91384-	Page 5 of 6
Applicant's/Registrant's Name & Address: CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	Product: T2.200 for Dogs	

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.1300	Acute inhalation toxicity				Waiver requested due product being liquid wit low volatility and maximum 4 mL as a single dose to skin of dogs
870.2400	Acute eye irritation	Submitted Dec 3, 2015	91639	PER	N-01986 - Non-GLP Acute Eye Irritation / Corrosion
870.2400	Acute eye irritation	Submitted Dec 3, 2015	91639	PER	B-01981 - Acute eye irritation / corrosion
870.2500	Acute dermal irritation	Submitted Dec 3, 2015	91639	PER	B-01980 - Acute dermal irritation
870.2600	Skin sensitization	Submitted Dec 3, 2015	91639	PER	E-01982 - Skin sensitization – Local lymph node assay
870.7200	Companion animal safety	Submitted Dec 3, 2015	91639	PER	CV-15-154 - Target Animal Safety Adults (>6 months old)
870.7200	Companion animal safety	Submitted Dec 3, 2015	91639	PER	CV-15-155 - Target Animal Safety Puppies (<7 we old)
157.20	Child-resistant packaging testing	49649301	74720	PER	Report KVS-201501
157.20	Child-resistant packaging testing	49649305	74720	PER	Report KVS-201505
157.20	Child-resistant packaging testing	49649308	74720	PER	Report KVS-201508
157.20	Child-resistant packaging testing	49649309	74720	PER	Report KVS-201509
157.20	Child-resistant packaging testing	49649310	74720	PER	Report KVS-201510

DATA MATRIX

Date: December 3, 2015	EPA Reg No./File Symbol: 91384-	Page 6 of 6
Applicant's/Registrant's Name & Address: CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	Product: T2.200 for Dogs	

Ingredient: permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
157.20	Child-resistant packaging testing	49649313	74720	PER	Report KVS-201513
157.20	Child-resistant packaging testing	49681401	74720	PER	Report KVS-201514
157.20	Child-resistant packaging testing	49681402	74720	PER	Report KVS-201515
157.20	Child-resistant packaging testing	49681403	74720	PER	Report KVS-201516
157.20	Child-resistant packaging testing	49719401	74720	PER	Report KVS-201517
157.20	Child-resistant packaging testing	49719402	74720	PER	Report KVS-201518
157.20	Child-resistant packaging testing	49719403	74720	PER	Report KVS-201521

DATA MATRIX

Date: **December 3, 2015**	EPA Reg No./File Symbol: **91384-**
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**
Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**	

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]			SEE SUBSEQUENT PAGES		

Signature:	Name and Title: John A. Tatum III, Chief Operating Officer	Date: 12-3-15

DATA MATRIX

Date: December 3, 2015

EPA Reg No./File Symbol: 91384-

Applicant's/Registrant's Name & Address:
CAP IM Supply, Inc.
303 Perimeter Center North Ste 300
Atlanta, GA 30346

Product:
T2.200 for Dogs

Ingredient: permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]			91639	PER	CV-15-143 Pilot study canine flea/tick
			91639	PER	CV-15-144 *Ixodes scapularis* (Deer ticks)
			91639	PER	CV-15-145 - *Dermacentor variabilis* (American dog ticks)
			91639	PER	CV-15-146 - *Rhipicephalus sanguineus* (Brown dog tick)
			91639	PER	CV-15-147 - *Amblyomma americanum* (Lone Star tick)
			91639	PER	CV-15-148 - *Aedes aegyptii* (mosquitoes)
			91639	PER	CV-15-149 - *Stomoxys calcitrans* (biting flies)
			91639	PER	CV-15-150 - Waterfastne. (repeated water immersion)
			91639	PER	CV-15-151 - Ovicidal and larvicidal fleas in dogs
			91639	PER	CV-15-152 - Control of fleas in the environment (carpets)
			91639	PER	CV-15-153 - Simulated home environment

DATA MATRIX

Date: **December 3, 2015**	EPA Reg No./File Symbol: **91384-**
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**
Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**	

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]			91639	PER	Literature review of eff of imidacloprid and permethrin against Chewing Lice, *Trichodectes canis*, infestations on dogs
			91639	PER	
			91639	PER	
			91639	PER	
			91639	PER	
			91639	PER	
			91639	PER	
			91639	PER	
			91639	PER	
			91639	PER	
			91639	PER	
					Not applicable -- product does not contain an oxidizing or reducing agent
			91639	PER	

DATA MATRIX

Date: **December 3, 2015**	EPA Reg No./File Symbol: **91384-**
Applicant's/Registrant's Name & Address: **CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346**	Product: **T2.200 for Dogs**

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]					Not applicable -- product potentially explosive
			91639	PER	
					Not applicable -- not an emulsifiable liquied to be diluted with petroleum solvent
			91639	PER	
					Not applicable -- not to be used around electrical equipment
			91639	PER	
			91639	PER	
			91639	PER	
					Not applicable -- not a water insoluble substance or fibrous substance
			91639	PER	B-01983 - Acute oral toxicity – Acute toxic class method
			91639	PER	B-01984 - Acute dermal toxicity

DATA MATRIX

Date: December 3, 2015	EPA Reg No./File Symbol: 91384-	Page 5 of 6
Applicant's/Registrant's Name & Address: CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	Product: T2.200 for Dogs	

Ingredient: permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
[redacted]					Waiver requested due t product being liquid with low volatility and maximum 4 mL as a single dose to skin of dogs
			91639	PER	N-01986 - Non-GLP Acute Eye Irritation / Corrosion
			91639	PER	B-01981 - Acute eye irritation / corrosion
			91639	PER	B-01980 - Acute dermal irritation
			91639	PER	B-01982 - Skin sensitization – Local lymph node assay
			91639	PER	CV-15-154 - Target Animal Safety Adults (>6 months old)
			91639	PER	CV-15-155 - Target Ani Safety Puppies (<7 wee old)
			74720	PER	Report KVS-201501
			74720	PER	Report KVS-201505
			74720	PER	Report KVS-201508
			74720	PER	Report KVS-201509
			74720	PER	Report KVS-201510

DATA MATRIX

Date: December 3, 2015	EPA Reg No./File Symbol: 91384- Page 6 of 6
Applicant's/Registrant's Name & Address: CAP IM Supply, Inc. 303 Perimeter Center North Ste 300 Atlanta, GA 30346	Product: T2.200 for Dogs

Ingredient: **permethrin (CAS No. 52645-53-1), pryiproxyfen (CAS No. 95737-68-1), and imidacloprid (CAS No. 138261-41-3)**

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
			74720	PER	Report KVS-201513
			74720	PER	Report KVS-201514
			74720	PER	Report KVS-201515
			74720	PER	Report KVS-201516
			74720	PER	Report KVS-201517
			74720	PER	Report KVS-201518
			74720	PER	Report KVS-201521

NOTE TO REVIEWER: [(Optional text appears in brackets and parenthesis - the final label may include some or all of the optional text on front, back, side, or inside label panels. Optional marketing claims: see lists at the end of the label)]

Label Directions and Container (Carton, Overwrap of 2 x 3-Count, 2 x 4-Count, 2 x 6-Count, and 3 x 4-Count Cartons), Package Insert, Blister, and Reminder Stickers for

3 x 0.014 FL. OZ. PACKAGE
3 x 0.034 FL. OZ. PACKAGE
3 x 0.084 FL. OZ. PACKAGE
3 x 0.135 FL. OZ. PACKAGE

4 x 0.014 FL. OZ. PACKAGE
4 x 0.034 FL. OZ. PACKAGE
4 x 0.084 FL. OZ. PACKAGE
4 x 0.135 FL. OZ. PACKAGE

6 x 0.014 FL. OZ. PACKAGE
6 x 0.034 FL. OZ. PACKAGE
6 x 0.084 FL. OZ. PACKAGE
6 x 0.135 FL. OZ. PACKAGE

8 x 0.014 FL. OZ. PACKAGE
8 x 0.034 FL. OZ. PACKAGE
8 x 0.084 FL. OZ. PACKAGE
8 x 0.135 FL. OZ. PACKAGE

(FRONT PANEL OF 2 x 3-COUNT, 2 X 4-COUNT, 2 X 6-COUNT, AND 3 X 4-COUNT OVERWRAP)

T2.200 for Dogs

Alternate Brand Names

[ADV Advecta for Dogs]
[ADV Advecta 2 for Dogs]
[ADV Advecta II for Dog
[ADV Advecta 3 for Dogs]
[ADV Advecta III for Dog
[ADV PetAction for Dogs]
[ADV PetAction 2 for Dogs]
[ADV PetAction II for Dogs]
[ADV PetAction 3 for Dogs]
[ADV PetAction III for Dogs]
[ADV PetLock for Dogs]
[ADV PetLock 2 for Dogs]
[ADV PetLock II for Dogs]
[ADV PetLock 3 for Dogs]
[ADV PetLock III for Dogs]
[Advecta 3 for Dogs]
[Advecta III for Dogs]
[Advecta ADV for Dogs]
[Advecta ADV 2 for Dogs]
[Advecta ADV II for Dogs]
[Advecta ADV 3 for Dogs]
[Advecta ADV III for Dogs]
[Advecta Complete for Dogs]
[Advecta Max for Dogs]
[Advecta Ticks for Dogs

[Advecta Tix for Dogs]]
[Advecta Total for Dogs]
[Advectix for Dogs]
[Advectix 2 for Dogs]
[Advectix II for Dogs]
[Advectix 3 for Dogs]
[Advectix III for Dogs]
[Para|Defense 3 for Dogs]
[Para|Defense Advanced for Dogs]
[Para|Defense Complete for Dogs]
[Para|Defense Extra for Dogs]
[Para|Defense Flea & Tick for Dogs]
[Para|Defense III for Dogs]
[Para|Defense Max for Dogs]
[Para|Defense Plus Tick Control for Dogs]
[Para|Defense Pro for Dogs]
[Para|Defense Plus Ticks for Dogs]
[Para|Defense Tix for Dogs]
[PetAction 3 for Dogs]
[PetAction III for Dogs]
[PetAction ADV for Dogs]
[PetAction ADV 2 for Dogs]
[PetAction ADV II for Dogs]
[PetAction ADV 3 for Dogs]
[PetAction ADV III for Dogs]
[PetAction Complete for Dogs]
[PetAction Max for Dogs]
[PetAction Ticks for Dogs]
[PetAction Tix for Dogs]
[PetAction Total for Dogs]
[PetLock 3 for Dogs]
[PetLock III for Dogs]]
[PetLock ADV for Dogs]
[PetLock ADV 2 for Dogs]
[PetLock ADV II for Dogs]
[PetLock ADV 3 for Dogs]
[PetLock ADV III for Dogs]
[PetLock Complete for Dogs]
[PetLock Max for Dogs]
[PetLock Ticks for Dogs]
[PetLock Tix for Dogs]
[PetLock Total for Dogs]

Monthly topical treatment and prevention of ticks, fleas, mosquitos, biting flies, and lice.
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 4-10 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 11-20 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 21-55 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing over 55 lbs.]

KEEP OUT OF REACH OF CHILDREN
WARNING

Active Ingredients	% By Weight
Imidacloprid	8.80%
Permethrin*	44.00%
Pyriproxyfen	0.44%
Other Ingredients	46.76%
Total	100.00%

*cis/trans ratio: Max 55(±) cis and min 45%(±) trans

See back panel for Precautionary Statements

See package insert for Directions for Use, Storage and Disposal, and First Aid information.

DO NOT USE ON CATS

Net Contents:

[2 cartons of [0.042 fl. oz.][0.056 fl. oz.][0.084 fl. oz.] ([3,4,6] applicators each containing 0.014 fl. oz (0.4 mL), [3,4,6] doses per carton, [6,8,12] doses total)]

[2 cartons of [0.102 fl. oz.][0.136 fl. oz.][0.204 fl. oz.] ([3,4,6] applicators each containing 0.034 fl. oz (1.0 mL), [3,4,6] doses per carton, [6,8,12] doses total)]

[2 cartons of [0.255 fl. oz.][0.34 fl. oz.][0.51 fl. oz.] ([3,4,6] applicators each containing 0.084 fl. oz (2.5 mL), [3,4,6] doses per carton, [6,8,12] doses total)]

[2 cartons of [0.405 fl. oz.][0.54 fl. oz.][0.81 fl. oz.] ([3,4,6] applicators each containing 0.135 fl. oz (4.0 mL), [3,4,6] doses per carton, [6,8,12] doses total)]

[3 cartons of [0.056 fl. oz.] (4 applicators each containing 0.014 fl. oz (0.4 mL), 4 doses per carton, 12 doses total)]

[3 cartons of [0.136 fl. oz.] (4 applicators each containing 0.034 fl. oz (1.0 mL)], 4 doses per carton, 12 doses total)]

[3 cartons of [0.34 fl. oz.] (4 applicators each containing 0.084 fl. oz (2.5 mL)], 4 doses per carton, 12 doses total)]

[3 cartons of [0.54 fl. oz.] (4 applicators each containing 0.135 fl. oz (4.0 mL)], 4 doses per carton, 12 doses total)]

(FRONT PANEL OF CARTON)

T2.200 for Dogs

Alternate Brand Names

[ADV Advecta for Dogs]
[ADV Advecta 2 for Dogs]
[ADV Advecta II for Dog
[ADV Advecta 3 for Dogs]
[ADV Advecta III for Dog
[ADV PetAction for Dogs]
[ADV PetAction 2 for Dogs]
[ADV PetAction II for Dogs]
[ADV PetAction 3 for Dogs]
[ADV PetAction III for Dogs]
[ADV PetLock for Dogs]
[ADV PetLock 2 for Dogs]
[ADV PetLock II for Dogs]
[ADV PetLock 3 for Dogs]
[ADV PetLock III for Dogs]
[Advecta 3 for Dogs]
[Advecta III for Dogs]
[Advecta ADV for Dogs]
[Advecta ADV 2 for Dogs]
[Advecta ADV II for Dogs]
[Advecta ADV 3 for Dogs]
[Advecta ADV III for Dogs]
[Advecta Complete for Dogs]
[Advecta Max for Dogs]
[Advecta Ticks for Dogs
[Advecta Tix for Dogs]]
[Advecta Total for Dogs]
[Advectix for Dogs]
[Advectix 2 for Dogs]
[Advectix II for Dogs]
[Advectix 3 for Dogs]
[Advectix III for Dogs]
[Para|Defense 3 for Dogs]
[Para|Defense Advanced for Dogs]
[Para|Defense Complete for Dogs]
[Para|Defense Extra for Dogs]
[Para|Defense Flea & Tick for Dogs]
[Para|Defense III for Dogs]
[Para|Defense Max for Dogs]
[Para|Defense Plus Tick Control for Dogs]
[Para|Defense Pro for Dogs]
[Para|Defense Plus Ticks for Dogs]
[Para|Defense Tix for Dogs]
[PetAction 3 for Dogs]
[PetAction III for Dogs]
[PetAction ADV for Dogs]
[PetAction ADV 2 for Dogs]
[PetAction ADV II for Dogs]
[PetAction ADV 3 for Dogs]
[PetAction ADV III for Dogs]
[PetAction Complete for Dogs]

[PetAction Max for Dogs]
[PetAction Ticks for Dogs]
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[PetAction Total for Dogs]
[PetLock 3 for Dogs]
[PetLock III for Dogs]]
[PetLock ADV for Dogs]
[PetLock ADV 2 for Dogs]
[PetLock ADV II for Dogs]
[PetLock ADV 3 for Dogs]
[PetLock ADV III for Dogs]
[PetLock Complete for Dogs]
[PetLock Max for Dogs]
[PetLock Ticks for Dogs]
[PetLock Tix for Dogs]
[PetLock Total for Dogs]

Monthly topical treatment and prevention of ticks, fleas, mosquitos, biting flies, and lice.

[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 4-10 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 11-20 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 21-55 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing over 55 lbs.]

KEEP OUT OF REACH OF CHILDREN
WARNING

Active Ingredients	% By Weight
Imidacloprid	8.80%
Permethrin*	44.00%
Pyriproxyfen	0.44%
Other Ingredients	46.76%
Total	100.00%

*cis/trans ratio: Max 55(±) cis and min 45%(±) trans

See back panel for Precautionary Statements
See package insert for Directions for Use, Storage and Disposal, and First Aid information.

DO NOT USE ON CATS

Net Contents:
[0.042 fl. oz.][0.056 fl. oz.][0.084 fl. oz.][0.112 fl. oz.] [3,4,6,8] applicators each containing 0.014 fl. oz (0.4 mL)]
[0.102 fl. oz.][0.136 fl. oz.][0.204 fl. oz.][0.272 fl. oz.] [3,4,6,8] applicators each containing 0.034 fl. oz (1.0 mL)]
[0.255 fl. oz.][0.34 fl. oz.][0.51 fl. oz.][0.68 fl. oz.] [3,4,6,8] applicators each containing 0.084 fl. oz (2.5 mL)]
[0.405 fl. oz.][0.54 fl. oz.][0.81 fl. oz.][1.08 fl. oz.] [3,4,6,8] applicators each containing 0.135 fl. oz (4.0 mL)]

(BACK PANEL OF CARTON AND OF OVERWRAP OF 2 X 3-COUNT, 2 X 4-COUNT, 2 X 6-COUNT, AND 3 X 4-COUNT CARTONS)

T2.200 for Dogs

Monthly topical treatment and prevention of ticks, fleas, mosquitos, biting flies, and lice.
[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing 4-10 lbs.]
[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing 11-20 lbs.]
[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing 21-55 lbs.]
[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing over 55 lbs.]
READ THE ENTIRE LABEL BEFORE EACH USE

Monthly topical treatment and prevention of ticks, fleas, mosquitos, biting flies, and lice on Dogs

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS
WARNING. Causes substantial but temporary eye injury. Do not get in eyes or on clothing. Harmful if swallowed. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Remove and wash contaminated clothing before reuse.

HAZARDS TO DOMESTIC ANIMALS
For external use on dogs only. Do not use on animals other than dogs. Do not use on puppies under seven (7) weeks of age [or weighing less than 4 pounds]. Do not get this product in dog's eyes or mouth. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing animals. Individual sensitivities, while rare, may occur after using ANY pesticide product for dogs. If signs persist, or become more severe, consult a veterinarian immediately. If your animal is on medication, consult your veterinarian before using this or any other product.

ENVIRONMENTAL HAZARDS
This pesticide is extremely toxic to aquatic organisms, including fish and invertebrates. Do not add directly to water. Do not contaminate water when disposing of product or packaging.

Side Effects:
Monitor your dog after application. Side effects, although very rare, may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as vomiting or diarrhea have also been reported. If these or other side effects (such as lethargy or agitation) occur, consult your veterinarian or call 1-855-844-4375.

DO NOT USE ON CATS – MAY BE FATAL. Keep cats away from treated dogs for 24 hours. If applied to a cat or ingested by a cat, contact your veterinarian immediately.

For consumer questions call 1-8XX-XXX-XXXX
For medical emergencies call 1-855-844-4375

CAP Supply, Inc.
303 Perimeter Center North, Suite 300
Atlanta, GA 30346

EPA Est. No. 74720-DEU-01

EPA Reg No. 91384-XXX

[Sample – Not for (Re)Sale]

[Store Use Only]

(SIDE PANELS OF CARTON AND OF OVERWRAP OF 2 X 3-COUNT, 2 X 4-COUNT, 2 X 6-COUNT, AND 3 X 4-COUNT CARTONS)

[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing 4-10 lbs.]
[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing 11-20 lbs.]
[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing 21-55 lbs.]
[For use only on Dogs and Puppies 7 Weeks of age and Older and Weighing over 55 lbs.]

[T2.200 for Dogs]

[EPA Reg. No. 91384-xxx]
Lot/Batch Number

Alternate Brand Names

[ADV Advecta for Dogs]
[ADV Advecta 2 for Dogs]
[ADV Advecta II for Dog
[ADV Advecta 3 for Dogs]
[ADV Advecta III for Dog
[ADV PetAction for Dogs]
[ADV PetAction 2 for Dogs]
[ADV PetAction II for Dogs]
[ADV PetAction 3 for Dogs]
[ADV PetAction III for Dogs]
[ADV PetLock for Dogs]
[ADV PetLock 2 for Dogs]
[ADV PetLock II for Dogs]
[ADV PetLock 3 for Dogs]
[ADV PetLock III for Dogs]
[Advecta 3 for Dogs]
[Advecta III for Dogs]
[Advecta ADV for Dogs]
[Advecta ADV 2 for Dogs]
[Advecta ADV II for Dogs]
[Advecta ADV 3 for Dogs]
[Advecta ADV III for Dogs]
[Advecta Complete for Dogs]
[Advecta Max for Dogs]
[Advecta Ticks for Dogs
[Advecta Tix for Dogs]]
[Advecta Total for Dogs]
[Advectix for Dogs]
[Advectix 2 for Dogs]
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[Para|Defense Pro for Dogs]
[Para|Defense Plus Ticks for Dogs]
[Para|Defense Tix for Dogs]
[PetAction 3 for Dogs]
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[PetAction Complete for Dogs]

[PetAction Max for Dogs]
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[PetLock Ticks for Dogs]
[PetLock Tix for Dogs]
[PetLock Total for Dogs]

Monthly topical treatment and prevention of ticks, fleas, mosquitos, biting flies, and lice.

[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 4-10 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 11-20 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing 21-55 lbs.]
[For use only on Dogs and Puppies 7 Weeks of Age and Older and Weighing over 55 lbs.]

Active Ingredients	% By Weight
Imidacloprid	8.80%
Permethrin*	44.00%
Pyriproxyfen	0.44%
Other Ingredients	46.76%
Total	100.00%

*cis/trans ratio: Max 55(±) cis and min 45%(±) trans

KEEP OUT OF REACH OF CHILDREN
WARNING

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS

WARNING. Causes substantial but temporary eye injury. Do not get in eyes or on clothing. Harmful if swallowed. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Remove and wash contaminated clothing before reuse.

HAZARDS TO DOMESTIC ANIMALS

For external use on dogs only. Do not use on animals other than dogs. Do not use on puppies under seven (7) weeks of age [or weighing less than 4 pounds]. Do not get this product in dog's eyes or mouth. As with any product, consult your veterinarian before using this product on debilitated, aged, pregnant or nursing animals. Individual sensitivities, while rare, may occur after using ANY pesticide product for dogs. If signs persist, or become more severe, consult a veterinarian immediately. If your animal is on medication, consult your veterinarian before using this or any other product.

ENVIRONMENTAL HAZARDS

This pesticide is extremely toxic to aquatic organisms, including fish and invertebrates. Do not add directly to water. Do not contaminate water when disposing of product or packaging.

Side Effects:

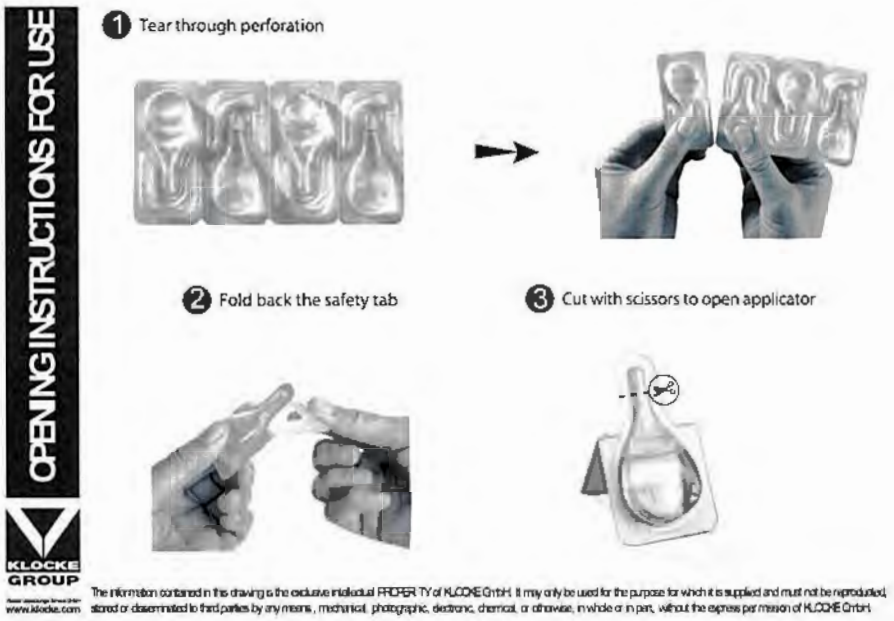
Monitor your dog after application. Side effects, although very rare, may include signs of skin irritation such as redness, scratching, or other signs of discomfort. Gastrointestinal signs such as vomiting or diarrhea have also been reported. If these or other side effects (such as lethargy or agitation) occur, consult your veterinarian or call 1-855-844-4375.

FIRST AID	
If In Eyes:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. • Call a poison control center or doctor for treatment advice.
If Swallowed:	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow • Do not induce vomiting unless told to do so by the poison control center or doctor. • Do not give anything to an unconscious person.
HOT LINE NUMBER	
Have the product container or label with you when calling a poison control center or doctor, or going for treatment. For medical emergencies call 1-855-844-4375. For consumer questions, call 1-888-846-4231	
NOTE TO PHYSICIAN	
Treat the patient symptomatically.	

DIRECTIONS FOR USE

It is a violation of Federal Law to use this product in a manner inconsistent with its labeling. Do not contaminate feed or food.

HOW TO OPEN



NOTE TO REVIEWER: When this product is packaged as the 3-count or 6-count version, the above image will show a 3-count applicator strip instead of the 4-count as shown above.

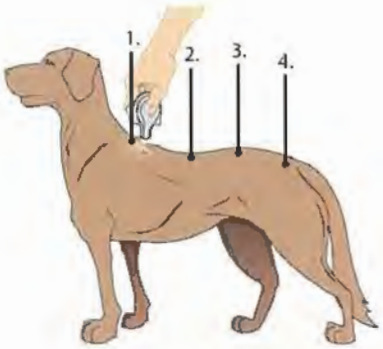
Repeat steps 1 to 3 for each applicator.

HOW TO APPLY

1. Prepare applicator as shown in "How to Open".
2. 4 – 10 lbs and 11-20 lbs. Apply the entire contents of the applicator to one spot as shown:

Part the hair on the dog back between the shoulder blades until the skin is visible. Place the tip of the applicator on the skin and gently squeeze to apply all the contents to the skin. Carefully avoid allowing the product to run off the side of the dog. Keep solution out of your dog's eyes and do not allow your dog to ingest this product.

21 – 55 lbs. and Over 55 lbs. Apply the entire contents of the applicator evenly to three or four spots on the top of the back of the dog from the shoulder to the base of the tail as shown:



At each application site part the hair of the dog until the skin is visible. Place the tip of the applicator on the skin and gently squeeze to apply the solution on the skin. Do not apply an amount of solution at any one spot that could cause some of the solution to run off the side of the dog. Keep solution out of your dog's eyes and do not allow your dog to ingest this product..

3. Discard empty applicator and packaging as described in the Storage and Disposal section.

4. Under normal conditions the product remains effective for a month. In cases of severe flea infestation, retreatment may be necessary earlier than one month. Do not reapply T2.200 more often than once every seven (7) days. Once flea control is attained, return to a monthly application schedule.

PRODUCT INFORMATION

The successive feeding activity of fleas on dogs may elicit a hypersensitivity skin disorder known as flea allergy dermatitis (FAD). Treatment of dogs with T2.200 rapidly kills fleas and may reduce the incidence of this condition.

T2.200 kills existing fleas on dogs within 12 hours. Reinfesting fleas are killed within 2 hours with protection against further flea infestation lasting at least four (4) weeks. Pre-existing pupae in the environment may continue to emerge for six (6) weeks or longer depending upon the climatic conditions.

Larval flea stages in the dog's surroundings are killed following contact with a T2.200 treated dog.

T2.200 is waterproof and remains effective following a shampoo treatment, swimming or after exposure to rain or sunlight.

Monthly treatments are required for optimal control and prevention of fleas and ticks.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

Pesticide Storage: Store in a cool, dry place. Protect from freezing. **Pesticide Disposal and Container Handling:** Non refillable container. **If empty:** Do not reuse this container. Place in trash or offer for recycling if available. **If partly filled:** Call your local solid waste agency for disposal instructions. Never place unused product down any indoor or outdoor drain.

LIMITED WARRANTY AND LIMITATION OF DAMAGES

IMPORTANT: READ BEFORE USE. Read the entire Directions for Use, Conditions of Warranties and Limitations of Liability before using this product. If these terms and conditions are not acceptable, return the unopened product container at once. By using this product, user or buyer accepts the following Disclaimer of Warranties and Limitations of Liability.

CONDITIONS: The directions for use of this product are believed to be adequate and must be followed carefully. However, it is impossible to eliminate all risks associated with the use of this product. Ineffectiveness, injury, and other unintended consequences may result because of such factors as manner of use or application (including misuse), the presence of other materials, weather conditions, and other unknown factors, all of which are beyond the control of CAP IM Supply, Inc.. All such risks shall be assumed by the user or buyer.

DISCLAIMER OF WARRANTIES: To the extent consistent with applicable law, CAP IM Supply, Inc. makes no other warranties, express or implied, of merchantability or of fitness for a particular purpose or otherwise, that extend beyond statements on this label.

LIMITATIONS OF LIABILITY: To the extent consistent with applicable law, neither CAP IM Supply, Inc., the manufacturer, nor the Seller shall be liable for any indirect, special, incidental or consequential damages resulting from the use, handling, application, storage, or disposal of this product. To the extent consistent with applicable law, the exclusive remedy of the user or buyer for any and all losses, injuries or damages resulting from the use, handling, application, or storage of this product, whether in contract, warranty, tort, negligence, strict liability or otherwise, shall not exceed the purchase price paid.

[For more information visit www. .com]

DO NOT USE ON CATS – MAY BE FATAL. Keep cats away from treated dogs for 24 hours. If applied to a cat or ingested by a cat, contact your veterinarian immediately.

For consumer questions call 1-8XX-XXX-XXXX
For medical emergencies call 1-855-844-4375

EPA Reg No. 91384-XXX

CAP Supply, Inc.
303 Perimeter Center North, Suite 300
Atlanta, GA 30346

(LABEL TEXT FOR INDIVIDUAL APPLICATOR)

T2.200 for Dogs

8.80% imidacloprid
44.00% permethrin
0.44% pyriproxyfen

EPA Reg. No. 91384-XXX

KEEP OUT OF REACH OF CHILDREN

WARNING

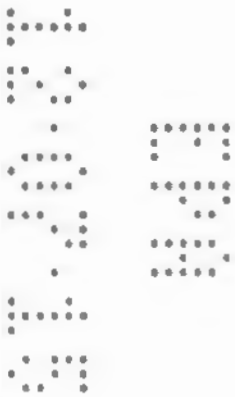
DO NOT USE ON CATS

Read the Entire Label Before Use

CAP IM Supply, Inc

[0.014 fl oz (0.4 mL)]
[0.034 fl oz (1.0 mL)]
[0.084 fl oz (2.5 mL)]
[0.135 fl oz (4.0 mL)]

Lot No. 0000000

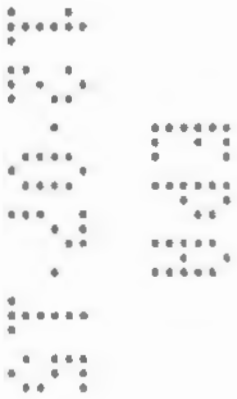


NOTE TO REVIEWER: [(Brackets and parentheses indicate alternate language)]

OPTIONAL MARKETING CLAIMS

- [For use on dogs and puppies 7 weeks of age and older]
- [T2.200 contains [imidacloprid], [permethrin] and [an/the] [insect growth regulator] [IGR] [pyriproxyfen]]
- [A single topical application remains effective for [a month][[four](4) weeks]]
- [Convenient, easy to apply [monthly] topical solution]
- [Once a month topical flea treatment for dogs 7 weeks of age or older]
- [T2.200 is indicated for the prevention and treatment of fleas, ticks, biting flies, mosquitoes, and lice on dogs 7 weeks of age and older]
- [Repels and kills ticks, fleas, and mosquitoes]
- [For the treatment and prevention of flea infestations]
- [One treatment prevents further flea infestations for [a month][[four](4) weeks]]
- [Kills fleas on dogs within 12 hours and continues to prevent infestations for [a month] [four](4) weeks]]
- [Repels and kills fleas before they lay eggs]
- [Larval flea stages in the dog's surroundings are killed following contact with T2.200 treated dogs]
- [Kills larval stages of fleas in the dog's environment following contact with T2.200 treated dogs]
- [Kills fleas within 12 hours of application].
- [Controls existing flea infestations by rapidly killing adult fleas]
- [Prevents reinfestations by killing adult fleas before they lay eggs]
- [Effectively breaks the flea life cycle]
- [Flea adulticide, larvicide and ovicide]
- [Prevents fleas on treated dogs from [infesting] [reinfesting] your home]
- [Effectively targets all [life] stages of [fleas] and [ticks]]
- [3-way flea protection [kills] [controls] adults, larvae, and eggs]
- [Prevents development of fleas, flea eggs, pupae and larvae for [a month][[four](4) weeks]]
- [Prevents development of all flea [life] stages [for] [a month][[four](4) weeks]]
- [Repels and kills [all] [life] [stages of fleas]]
- [Prevents flea eggs [and flea larvae] from developing into [biting] [adult] fleas]
- [Treatment with T2.200 rapidly kills fleas and may reduce the incidence of Flea Allergic Dermatitis (FAD)]
- [Repels and kills ticks including Deer ticks (vector of Lyme disease), American dog ticks (vector of Rocky Mountain spotted fever), Brown dog ticks (vector of Ehrlichiosis), and Lone Star ticks (vector of Ehrlichiosis) for up to four weeks]
- [Repels and kills mosquitoes for up to four weeks]
- [Repels and kills mosquitoes often before they have a chance to take a blood meal]
- [[Prevents blood-feeding by] [Kills and repels] mosquitoes]
- [Repels and inhibits blood-feeding by biting flies]
- [Repels and prevents blood-feeding by biting flies]
- [Repels [annoying][bothersome][nuisance] biting flies]
- [Inhibits [annoying][bothersome][nuisance] biting flies]
- [[Prevents][inhibits] blood-feeding by biting flies]
- [Remains effective after bathing and/or swimming]
- [Remains effective following swimming and/or shampooing]
- [Kills [biting][chewing] lice]
- [For treatment and prevention of [biting][chewing] lice [infestations]]
- [Controls existing [biting][chewing] lice infestations]
- [5-way protection against fleas, ticks, biting flies, mosquitoes, and lice]

- [Treats, prevents and controls [biting][chewing] lice [infestations]]
- [Provides effective control of [biting][chewing] lice [infestations]]
- [Kills [biting][chewing] lice and prevents further infestations]
- [For treatment and prevention of infestations with [biting][chewing] lice]
- [Waterproof]
- [Remains effective after exposure to rain or sunlight]
- [Fragrance free]
- [Contains the same active ingredients imidacloprid, pyriproxyfen and permethrin found in Bayer K9 Advantix II].
- [Contains the [same] active ingredients [found] [used] in [Bayer] K9 Advantix II]
- [T2.200 for Dogs is not manufactured by or distributed by Bayer Health Care LLC]
- [K9 Advantix II is a registered trademark of Bayer Health Care LLC]
- [Contains imidacloprid, pyriproxyfen and permethrin, the same active ingredients used in Bayer K9 Advantix II]
- [Compare to Bayer K9 Advantix II; Contains the same active ingredients as Bayer K9 Advantix II]
- [T2.200 is not manufactured by or distributed by Bayer Health Care LLC. K9 Advantix II is a registered trademark of Bayer Health Care LLC]
- [3 Pack [3 Applicators][3 Months Supply][3 Doses]]
- [4 Pack [4 Applicators][4 Months Supply][4 Doses]]
- [6 Pack [6 Applicators][6 Months Supply][6 Doses]]
- [8 Pack [8 Applicators][8 Months Supply][8 Doses]]
- [12 Pack [12 Applicators][12 Months Supply][12 Doses]]
- [3 Applications]
- [4 Applications]
- [6 Applications]
- [8 Applications]
- [12 Applications]
- [Buy [2,3,4,5,6,7,8,9,10] doses, get [1,2,3,4] free]
- [Small Dog [4-10 lbs.]]
- [Medium Dog [11-20 lbs.]]
- [Large Dog [21-55 lbs.]]
- [Ex Large Dog [Over 55 lbs.]]
- [Illustration of flea life cycle] [halts life cycle of fleas]
- [Illustration of tick life cycle] [halts life cycle of ticks]
- [Illustration of louse life cycle] [halts life cycle of lice]
- [Illustration of chewing lice life cycle] [halts life cycle of chewing lice]
- [Illustration of adult fleas] [kills adult fleas]
- [Illustration of flea eggs] [stops hatching of flea eggs[in the environment]]
- [Illustration of flea larvae] [stops development of flea larvae[in the environment]]
- [Illustration of chewing lice] [kills chewing lice]
- [Illustration of tick] [kills[and repels] ticks]
- [Illustration of flea] [kills fleas]
- [Illustration of louse] [kills lice]
- [Illustration of mosquito] [kills[and repels] mosquitos[and biting flies]]
- [5-way protection] 'Note to reviewer: To be associated with the 5 parasite illustrations.'
- [Picture or illustration of a dog or puppy of appropriate weight class]
- [Picture or illustration of the T2.200 logo]
- [Picture or illustration of the primary package, applicator tubes, pipettes]



(TEXT FOR REMINDER STICKERS)

[**Optional marketing claims**]

[Picture of Dog or Puppy 7 weeks or older]

[Picture of flea] [kills fleas]

[Picture of tick] [kills [and repels]ticks]

[Picture of chewing lice] [kills lice]

[Picture of mosquitoes] [kills [and repels]mosquitoes[and biting flies]]

[Quick-acting]

[Long-lasting]

[Does not wash off]

[For monthly control of fleas, ticks, chewing lice, mosquitoes]

[Optional Bar Code]

T2.200 for Dogs

The first time you treat your dog, place the First Application Sticker on your calendar. Apply Stickers [2 and 3] [2, 3, 4] [2 through 6] [2 through 8]to the calendar [30 and 60 days] [30, 60, and 90 days] [30, 60, 90, 120, and 150 days] [30, 60, 90, 120, 150, 180, and 210 days] [at the end of each 30 day period] after the first application to remind you it's time to reapply T2.200 for Dogs.

First Application Sticker: Apply T2.200 for Dogs
Month 2 Sticker: Apply T2.200 for Dogs
Month 3 Sticker: Apply T2.200 for Dogs
[Month 4 Sticker: Apply T2.200 for Dogs]
[Month 5 Sticker: Apply T2.200 for Dogs]
[Month 6 Sticker: Apply T2.200 for Dogs]
[Month 7 Sticker: Apply T2.200 for Dogs]
[Month 8 Sticker: Apply T2.200 for Dogs]

Do Not Use on Cats

For Customer Service please call 1-8xx-xxx-xxxx.

CAP Supply, Inc.
303 Perimeter Center North, Suite 300
Atlanta, GA 30346

[Optional bar code]

Certification with Respect to Label Integrity

version: 9/11/02

I certify that the information (including, but not limited to, text, tables, and graphics) contained in the electronic file identified below by file name and submitted with this certification is the same information as that on the paper copies of these documents included with this submission.

PROPOSED LABEL

EPA Registration #	Date Submitted to EPA	Electronic file name
91384-	December 3, 2015	091384-xxxxx.20151203.T2.200 for Dogs.PDF

I certify that the statements that I have made on this form are true, accurate, and complete. I acknowledge that any knowingly false or misleading statements may be punishable by fine or imprisonment or both under applicable law.

Signature

12-3-15
Date

John A. Tatum III
Name (typed)

Chief Operating Officer
Title

Inert ingredient information may be entitled to confidential treatment

INERT CLEARANCE STATUS FORM

Reviewer Name: Stephanie Varner			Request Date: Dec 17, 15
Tel: 703-347-0240	ISB	CUBE: S-4813	MAIL CODE:

A. COMMENTS:

The submitter has said that they will speak with the PM directly to resolve this issue.

B. PESTICIDE PRODUCT INFORMATION:

Receipt Number: 978275 EPA Reg. No/File Symbol: 91384-G Product Name: T2.200 for Dogs	Date on CSF: Dec 3, 15 Formulation:	Food-Use Pesticide: [] Yes [X]No

C. INGREDIENT INFORMATION:

Ingredient No.1	**Tolerance Exemption(s)[1]** 910	920	930	940	950	960
Chem. Name:						
Trade Name: [redacted]						
CAS Reg. No.:						

Comments: [redacted] is not listed in the Agency database. Please provide a manufacture letter (with letterhead) providing full compositional information including the manufacturer, constituent names, CAS numbers, and weight/weight percentage composition (100% composition).

Reviewer Name: Stephanie Varner **Review Date: 12/17/15**

[1] *Language from the Code of Federal Regulations (40 CFR 180, subpart D):*
40 CFR 180.910: Inert ingredients used pre- and post-harvest; 40 CFR 180.920: Inert ingredients used pre-harvest; 40 CFR 180.930: Inert ingredients applied to animals; 40 CFR 180.940: Tolerance exemptions for active and inert ingredients for use in antimicrobial formulations; 40 CFR 180.950: Tolerance exemptions for minimal risk active and inert ingredients; and 40 CFR 180.960: Polymers.

Pages 263-268 - *Confidential Statements of Formula may be entitled to confidential treatment*